SHIFTING AND SUSTAINED ATTENTION DEFICITS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

By

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Research indicates that children with Attention-Deficit/Hyperactivity Disorder (ADHD) have difficulty with tasks sensitive to frontal lobe dysfunction, such as sustaining attention for extended periods. However, less is known about the ability of these children to shift their attention between cognitive sets, a task previously shown to be sensitive to cerebellar dysfunction. Additionally, research that has attempted to localize the neuroanatomical dysfunction in children with ADHD remains inconclusive as researchers have found dysfunction in multiple regions, including the frontal lobes, subcortical structures, and cerebellum. In order to help elucidate the neuroanatomical areas of dysfunction in children with ADHD, this study compared the performance of children diagnosed with pure ADHD to normal control children on computerized measures of sustained and shifting attention. In addition, these two groups of children were compared on a second measure previously shown to be sensitive to frontal lobe dysfunction (i.e., the Stroop test) and on a second measure previously shown to be

sensitive to cerebellar dysfunction (i.e., analysis of smooth pursuit eye-movements). Children with ADHD performed significantly worse than normal controls on both the computerized sustained and shifting attention measures. However, significant differences were not found between the two groups on the Stroop test or on a measure of anticipatory saccades during smooth pursuit. Results of a discriminant function analysis indicated that the computerized sustained and shifting attention tasks were robust and sensitive and together correctly classified 80% of the subjects. Overall, children with ADHD performed significantly worse than normal control children on one measure sensitive to frontal lobe dysfunction and one measure sensitive to cerebellar dysfunction. Specifically, results of this study indicate that in addition to having difficulty sustaining attention, children with ADHD are impaired in their ability to quickly shift their attention between cognitive sets. Alternatively, the performance of the two groups was similar on the other measures of frontal lobe and cerebellar functioning. Further research remains necessary to improve our understanding of the neuroanatomical underpinnings of ADHD.

CHAPTER 1
INTRODUCTION

Numerous studies have been conducted to elucidate the dysfunction in children diagnosed with Attention-Deficit/Hyperactivity Disorder (ADHD). These studies have been inconsistent in their usage of a pure ADHD population versus children diagnosed with ADHD and other behavioral, emotional, and/or academic problems. While research has supported the hypothesis that children with ADHD have difficulty sustaining attention for extended periods of time, less is known about the specific ability of these children to shift their attention between cognitive sets. These sustained and shifting attention abilities have been evaluated in non-ADHD populations (including normal controls and patients with neuroanatomical lesions) and have been shown to be sensitive to frontal lobe and cerebellar functioning, respectively. Furthermore, research that has attempted to localize the neuroanatomical dysfunction of ADHD to specific brain regions remains inconclusive. Therefore, in an attempt to support the hypothesis that ADHD results from dysfunction to frontal-subcortical-cerebellar pathways, the current study proposed to compare children diagnosed with pure ADHD (according to current criteria) to normal control subjects on measures of sustained and shifting attention, as well as other cognitive and neurological tests known to be sensitive to frontal lobe and cerebellar dysfunction. The next section includes a discussion of ADHD and its diagnostic criteria, comorbid diagnoses, associated executive functioning, and neuroanatomical abnormalities. A discussion of the neuroanatomy of the cerebellum and its associated

nonmotor functions is also included. Finally, a discussion of the neuroanatomy that links the frontal lobes to the cerebellum is presented as the hypothesized substrate underlying dysfunction in ADHD.

Attention-Deficit/Hyperactivity Disorder

History of the Disorder

Attention-Deficit/Hyperactivity Disorder (ADHD) is the diagnostic label currently used to describe a heterogeneous group of children and adults who display significant problems of inattention, impulsiveness, and/or hyperactivity. Though ADHD is one of the most prevalent childhood psychiatric disorders today, references to a proximity of the disorder did not appear in scientific reference until the turn of the century. At that time, George Still published lectures in Europe on his clinical observations of children who showed symptoms of defiance, aggressiveness, emotional intensity, inattentiveness, and disinhibition (Still, 1902). He noted impulsiveness or an inability to delay gratification as the primary attribute of these children. Still described the children as displaying a defect in the moral regulation of their behavior. Though Still believed that some children displayed poor impulse control as a result of inadequate upbringing, he hypothesized that children with inadequate upbringing could be differentiated from those whose deficient moral control resulted from a neurological deficiency (e.g., neuronal cell modification, cortical disconnection, or a decreased threshold for inhibition of responding).

Interest in ADHD extended to the United States, sparked by an outbreak of encephalitis and secondary reports of cognitive and behavioral problems in children surviving the illness. Again, symptoms such as impulsivity, inattention, and disinhibition

were described in what came to be termed Postencephalitic Behavior Disorder (Barkley, 1998). This clear connection between acquired brain damage and socially disruptive behavior problems led to a proliferation of research in the 1930s into other medical disorders, such as epilepsy and head injury, which were also thought to secondarily result in similar behavior problems. Again, studies found that children displayed a variety of cognitive and behavioral impairments including inattention, impulsiveness, and hyperactivity. This link between brain damage and secondary behavior problems eventually led to the use of the term Minimal Brain Dysfunction (MBD).

During the next few decades, interest in understanding the neurological mechanisms of these childhood behavior problems continued to grow. Laufer is attributed with being one of the first researchers to hypothesize that a specific central nervous system (CNS) deficit (i.e., overstimulation of the cortex due to a lowered threshold for stimulation in the thalamus) may account for some of the behavioral symptomatology seen in these children (Barkley, 1998). Though other researchers in this area included inattention as a symptom of the disorder, Laufer's studies focused primarily on children who displayed hyperactivity (Laufer & Denhoff, 1957). Consistent with the focus on hyperactivity at this time, Hyperkinetic Reaction of Childhood became the diagnosis used in the second edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-II; American Psychiatric Association, 1968).

The next diagnostic schema set forth by the third edition of the Diagnostic and Statistical Manual for Mental Disorders (DSM-III; American Psychiatric Association, 1980) formally recognized deficits in sustained attention and impulse control, in addition to hyperactivity, as defining features of the childhood behavior disorder. The DSM-III

recognized the diagnosis of Attention Deficit Disorder (ADD) and included two subtypes, with or without hyperactivity (ADD+H, ADD-H). The emergence of this shift away from an exclusive focus on hyperactivity has been attributed to the research and subsequent model of attention deficits proposed by Virginia Douglas and her colleagues at McGill University in Canada (Barkley, 1998). Though research did exist to support the view that in addition to hyperactivity, inattention was a primary feature of the disorder, little evidence existed at the time of formulation to support the development of discrete subtypes. Due to this lack of scientific evidence for subtypes during the inception of the DSM-III-R (American Psychiatric Association, 1987), the diagnostic criteria for Attention Deficit Disorder without hyperactivity were no longer officially recognized, and a single set of diagnostic criteria for Attention-Deficit Hyperactivity Disorder were proposed. Therefore, the research conducted on children with ADHD according to DSM-III-R criteria fails to differentiate among any subtypes.

Current Diagnostic Criteria

After publication of the DSM-III-R, research was mounting that did support the subtyping of ADD into those with and without hyperactivity. Differences in areas such as activity level, associated achievement difficulties, and level of aggression were emerging as characteristic differences between those with ADD+H and ADD-H. Therefore, in the fourth edition of the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV), the nomenclature for the disorder was again divided into subtypes (American Psychiatric Association, 1994). In this most recent edition, three subtypes of ADHD are recognized: ADHD-predominantly inattentive type, ADHD-predominantly

hyperactive type, and ADHD-combined type. Symptoms of inattention include the following:

- Failure to give close attention to details or making careless mistakes in schoolwork or other activities.
- Difficulty sustaining attention in tasks or play activities.
- Not seeming to listen when spoken to directly.
- Not following through on instructions.
- Failure to finish schoolwork, chores, or duties in the workplace.
- Difficulty organizing tasks and activities.
- Avoiding, disliking, or being reluctant to engage in tasks that require sustained mental effort.
- Losing things necessary for tasks or activities.
- Being easily distracted by extraneous stimuli.
- Forgetfulness in daily activities.

In order to be diagnosed with ADHD-predominantly inattentive type, six or more of the aforementioned symptoms must have been present before 7 years of age, must have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level, and must be present in at least two settings. Symptoms of hyperactivity/impulsivity include the following:

- Fidgeting with hands or feet or squirming in one's seat.
- Leaving one's seat in the classroom or in other situations in which remaining seated is expected.

- Running about or climbing excessively in situations in which it is inappropriate or subjectively feeling restless.
- Having difficulty playing or engaging in leisure activities quietly.
- Being "on the go" or acting as if "driven by a motor".
- Talking excessively.
- Blurting out answers before questions have been completed.
- Having difficulty awaiting one's turn.
- Interrupting or intruding upon others.

Criteria for ADHD-predominantly hyperactive/impulsive type are similar to those for predominantly inattentive type, though they refer to the symptoms of hyperactivity/impulsivity. Children diagnosed with ADHD-combined type meet criteria for both inattentive type and hyperactive/impulsive type.

Prevalence in Children

Attention-deficit/hyperactivity disorder is one of the most prevalent mental disorders of childhood. Research that furthers our understanding of the mechanisms and associated deficits of this disorder is critical as approximately 50% of referrals to childhood mental health services are currently accounted for by ADHD. A review by Greenhill (1998) of epidemiologic studies across a variety of countries indicated that the rates for ADHD (including all subtypes) range between 1.7% and 12.6%. National prevalence estimates for ADHD in the United States vary between 3% and 5% for school age children, with four to nine times as many boys as girls diagnosed (American Psychiatric Association, 1994). ADHD is typically viewed as a developmental disability, with symptoms frequently first observed when children are toddlers. Although some

individuals report continued ADHD symptomatology into adulthood, research indicates that most people report a decrease in symptoms beginning at age 10. Symptoms of hyperactivity are reported to decline more quickly than symptoms of impulsivity or inattention (Goldman, Genel, Bezman, & Slanetz, 1998). A review of studies suggests that the population rates of ADHD decline by approximately 50% for every 5 years of age, leading to estimates of 0.8% in 20-year-olds and 0.05% in 40-year-olds (Greenhill, 1998).

Comorbid Diagnoses

It has been reported that up to two-thirds of clinically referred school-age children with ADHD meet diagnostic criteria for another disorder. These comorbid disorders include, but are not limited to, Oppositional Defiant Disorder (ODD), Conduct Disorder (CD), Learning Disability (LD), depression, and/or anxiety (Biederman, Newcorn, & Spirch, 1991). Research suggests an approximate 50% overlap between ADHD and the disruptive behavior disorders of ODD and CD, though comorbidity rates as high as 93% have been found (Carlson, Tamm & Gaub, 1997; Jensen, Martin, & Cantwell, 1997; Nigg, Hinshaw, Carte, & Treuting, 1998; Szatmari, Boyle, & Offord, 1989). With regard to these disruptive behavior disorders, also termed externalizing disorders, population-based studies suggest that children diagnosed with both ADHD and an externalizing disorder are at the greatest risk for poor long-term outcomes such as increased delinquent behaviors and poor scholastic achievement (Moffitt & Silva, 1988).

Though the comorbidity rates reported for mood disorders in children with ADHD are slightly lower than the rates reported for comorbid disruptive behavior disorders, the reported overlap between them remains significant at an average of 25%

(range = 3-75%; Biederman et al., 1991; Jensen et al., 1997). The mood disorders seen in children with ADHD include dysthymia, major depression, bipolar disorder, and overanxious disorder.

Reported rates of comorbidity between ADHD and learning difficulties have been highly variable, ranging from as low as 10% to as high as 92% (Biederman et al., 1991; Cantwell & Baker, 1991; Dykman & Ackerman, 1991; Riccio, Gonzalez & Hynd, 1994). The variability in findings likely results from the use of different definitions of learning difficulty, including speech and language impairment, reading disability, mathematics disability, nonverbal learning disability, and general learning disability. Furthermore, with regard to general learning disability, criteria vary as follows:

- "A disorder in one or more of the basic psychological processes involved in understanding or in using language, spoken or written" (U.S. Public Law 94-142).
- Less than or equal to the 6th percentile of a spelling subtest of an achievement test.
- A reading quotient less than .85 with a reading percentile less than 25
- Greater than or equal to 1 ½ years between expected and actual reading level (Felton & Wood, 1989; Korkman & Pesonen, 1994; Nigg et al., 1998; Robins, 1992).

Cantwell and Baker (1991) suggested that while significant overlap is likely among subjects diagnosed with ADHD across the various DSM revisions, less overlap is likely across studies in those meeting diagnostic criteria for LD because of the high variability in definitions used. Furthermore, research specifically addressing the issue shows that the rates of comorbidity among ADHD and LD depend on the definition of LD used (Semrud-Clikeman et al., 1992). Specifically, high rates of comorbidity (38%) between ADHD and LD were found using a liberal definition of LD (i.e., reading and

arithmetic achievement test scores ≥ 10 standard score points below full scale IQ). Alternatively, the most stringent LD definition, which resulted in only a 17% comorbidity rate with ADHD, was stated as a score ≤ 85 standard score points on reading and arithmetic achievement tests and ≥ 1 standard score points below full scale IQ. Recognizing the importance of the use of a stringent definition of LD within ADHD populations, recent studies relied on the actual-expected achievement discrepancy score to define learning disability (Seidman et al., 1995). Nonetheless, Barkley (1998) called for the use of an even more a rigorous definition of LD based on both a discrepancy between predicted and actual achievement scores and a cut-off score (e.g., LD is defined as a discrepancy of ≥ 15 points between expected and actual achievement scores and a score ≥ 1.5 standard deviations below the mean on an achievement test).

Assessment Methodologies

As previously stated, researchers believe that even under the various DSM revisions, there is likely to be significant overlap of criteria used to diagnosis children with ADHD. Nonetheless, a variety of methodologies continue to be employed in the diagnostic process. Barkley and Edwards (1998) proposed that several components should be included in any comprehensive ADHD evaluation. These components include a (structured) clinical interview, parent, teacher, and/or self-report behavior rating scales, a medical/neurologic examination, neuropsychological testing, and behavioral observations (Barkley & Edwards, 1998).

Although using a variety of components serves to maximize diagnostic accuracy, numerous studies fail to implement this approach. Rather, ADHD is frequently diagnosed solely based on one of the proposed components, including symptom

checklists, rating scales, or structured interviews (Aylward, Verhulst, & Bell, 1990; Douglas & Benezra, 1990; Dykman & Ackerman, 1991; Felton & Wood, 1989; Grodzinsky & Diamond, 1992; Korkman & Pesonen, 1994). On the other hand, some recent studies have confirmed ADHD diagnoses using DSM symptom checklists as well as diagnostic interviews and/or rating scales (Faraone et al, 1993; Mataro, Garcia-Sanchez, Junque, Estevez-Gonzalez, & Pujol, 1997; Nigg et al., 1998; Reader, Harris, Schuerholz, & Denckla, 1994; Robins, 1992). The importance of using multiple diagnostic methodologies and stringent criteria was highlighted by Barkley (1998) who showed that changing cut-off criteria on structured interviews or rating scales from 1.5 to 2 standard deviations above the mean reduces the prevalence rates of ADHD in the population from an average of 14% to 2-9%. Structured interviews commonly used include the Diagnostic Interview for Children and Adolescents (DICA), the Schedule for Affective Disorder and Schizophrenia for Children (Kiddie SADS), and the Divergent and Convergent Interview. Two of the most frequently used rating scales are the Conners Rating Scales (Conners, 1997b) and the Child Behavior Checklist (CBCL; Achenbach, 1991). Both rating scales are available in parent, teacher, and self-report formats and provide a profile of the frequency/intensity of problematic behaviors. The diagnostic accuracy of the Attention Problems subscale of the CBCL was recently supported in a series of studies which found that this subscale showed excellent convergence with the diagnosis of ADHD as made through a structured interview, and this subscale had the highest discriminating power for ADHD among a variety of measures (Biederman et al., 1993; Chen, Faraone, Biederman, & Tsuang, 1994). The Conners Rating Scales have also been shown to discriminate among a group of adolescents with ADHD, adolescents

with emotional problems as rated by a psychiatrist, and a nonclinical control group (Conners 1997a). Table 1 lists the various methodologies used to diagnose ADHD across studies evaluating neurobehavioral functions in children diagnosed with the disorder.

Cognitive Functions

One of the components necessary in a comprehensive ADHD evaluation is neuropsychological testing. A common reason for initiating a neuropsychological evaluation is to assess for the cause of academic underachievement. Although poor school performance is often found among children with ADHD, a variety of factors, including inability to sit still without disrupting others, attend to the teacher, follow through on instruction, or organize their actions may be predictive of underachievement (Barkley, 1998). Alternatively, as ADHD has been shown to overlap frequently with LD it is often necessary to evaluate for reading, writing, and mathematics learning disabilities in children with ADHD who evidence academic difficulties (Semrud-Clikeman et al., 1992). Poor school performance may also be a direct result of low intellectual functioning rather than poor achievement. However, intellectual disability in ADHD may be due to deficient intellectual capability associated with comorbid disorders (e.g., conduct disorder; Frost, Moffit, & McGee, 1989). Research has specifically addressed this issue by assessing subsamples of children with ADHD: ADHD + CD, ADHD + major depressive disorder, ADHD + two or more anxiety disorders, and ADHD alone (Faraone, et al., 1993). Results showed that the undivided proband of ADHD subjects (N = 140) differed significantly from controls on Verbal and Performance IQ subtests and on an estimated Full Scale IQ score. Results also showed that the ADHD only subgroup (N = 64) significantly differed from controls on the same measures.

Table 1
ADHD Diagnostic Methodologies

Authors, year of publication	DSM checklists	Symptom questionnaires or rating scales	Structured interviews
Aylward, Verhlst, & Bell, 1990	Parent or teacher report of symptoms		
Barkley, Grodzinsky, & DuPaul, 1992	Empirical criteria		
Biederman et al., 1993			DSM[a]-III-R based structured interview Kiddie SADS[b]-E
Boucugnani & Jones, 1989		CBCL[c] [Inattentive Scale > 25(male) 22(female)] Bristol Social Adjustment Guides (Inconsequence Scale > 9) Conners (Hyperactivity Index > 15)	
Como, Bothe, Sulkes, & Kurlan, 1991	DSM[a]-III-R diagnostic criteria		
Denckla & Rudel, 1978		Conners rating scale for drug studies (>16 of 27 points on both parent and teacher ratings of hyperactivity items)	
Douglas & Benezra, 1990		Conners Abbreviated and Teacher (Hyperactivity Index > 1.5 S.D. above mean)	
Dykman & Ackerman, 1991			DICA[d]: Attention items
Faraone et al., 1993	Parent report of DSM[a]-III-R symptoms		Kiddie SADS[b]-E
Felton & Wood, 1989			DICA[d]: ADD items
Frost, Moffitt, & McGee, 1989		Revised Behavior Problem Checklist (>1 s.d above mean on Attention Problems Rutter Child Scale B (Inattention subscale > 1 S.D. above mean)	DISC[e]

Table 1 - continued

Authors, year of publication	DSM checklists	Symptom questionnaires or rating scales	Structured interviews
Grodzinsky & Diamond, 1992	DSM[a]-III-R diagnostic criteria	CAP[f] (≥ 93%ile; >1.5 S.D. above mean)	
Korkman & Pesonen, 1994	4 or 5 out of 5 points for > 6 of 12 DSM[a]-III attention items		
Loge, Staton, Beatty, 1990	DSM[a]-III-R diagnostic criteria		
Mataro, Garcia-Sanchez, Junque, Esteves-Gonzalez, Pujol, 1997	School psychologist rating of DSM[a]-III-R criteria Family interview of DSM[a]-III-R symptoms	Conners Teacher	Family interview of DSM[a]-III-R symptoms
McGee, Williams, Moffitt, & Anderson, 1989	Parent and teacher report of DSM[a]-III criteria	Rutter Child Scale B Revised Prob. Behavior Checklist (Attention Problems Subscale ≥ 8, ≥ 1 S.D. above mean)	DISC-C[e]
Mikkelsen, Brown, Minichiello, Millica, & Rapoport, 1982		Conners Teacher (factors I or IV > 2 S.D. above mean)	
Nigg, Hinshaw, Carte, & Treuting, 1998	DSM[a]-III-R Disruptive Behavior Disorder Checklist	Conners Abbreviated Symptom Questionnaire CBCL[c] (Attention Problems subscale)	Divergent and Convergent Interview
Reader, Harris, Schuerholz, & Denckla, 1994	Parent rating on DuPaul Scale of DSM[a]-III-R criteria	Conners Parent (Impulsivity/ Hyperactivity Factor T-score > 60) or CBCL[c] (Hyperactivity Scale T-score > 60)	
Robins, 1992	Parent checklist of DSM[a]-III-R criteria	Conners Teacher (Hypeactivity Scale > 2 S.D. above mean)	
Seidman, Biederman, Farone, Weber, & Oullette, 1997			Kiddie SADS[b]-E
Semrud-Clikeman, et al., 1992	DSM[a]-III criteria according to parent, child, and teacher interviews		

Table 1 - continued

Authors, year of publication	DSM checklists	Symptom questionnaires or rating scales	Structured interviews
Szatmari, Boyle, Offord, 1989		Items from the parent, teacher, and/or youth CBCL[c]	
Voeller & Heilman, 1988	DSM[a]-III criteria		
Weyandt & Willis, 1994	DuPaul Rating Scale of DSM[a]-III-R criteria DSM[a]-III-R Criteria according to pediatrician	Conners Parent and Teacher (1.5 S.D. above mean)	

[a]DSM = Diagnostic and Statistical Manual for Mental Disorders;
[b]SADS =
[c]CBCL = Child Behavior Checklist; Conners = Conners' Rating Scales
[d]DICA = Diagnostic Interview for Children and Adolescents;
[e]DISC-C = Diagnostic Interview Schedule for Children-Child Version;
[f]CAP = Children's Attention Profile (short form of CBCL-Teacher);

While their research suggested that psychiatric comorbidity may exacerbate intellectual impairments, pure ADHD is not without significant risk for school difficulties/failure (e.g., need for academic tutoring, repeating a grade, placement in a special class). The results from this body of research highlight the importance of evaluating for the presence of comorbid diagnoses that can skew results in studies of the neurocognitive abilities of children with ADHD.

Executive Functions

Beyond assessing intellectual and achievement abilities, neuropsychological tests are often administered to assess attentional capacity, level of distractibility, and planning/ organizational ability in children with ADHD. Higher cognitive components, including attending, maintaining set, regulating behavior, planning, and organizing, have been subsumed under the term executive function. As Denckla (1996) notes, "Executive

function comprises the planning and carrying out of sequences of nonautomatic responses that are produced in conformity not to the immediate environment but to some supraordiante goal." Knowledge of a child's executive abilities is particularly useful in developing appropriate educational recommendations, such as increased structure or supervision. Attentional batteries have also been shown to be useful in distinguishing children with a primary diagnosis of ADHD from those with inattentive, hyperactive, or impulsive behaviors secondary to another neurological disorder (e.g., Tourrette's syndrome; Como, Bothe, Sulkes, & Kurlan, 1991). Nonetheless, the assessment of executive function is not routinely included in ADHD diagnostic evaluations (Como, 1997).

A number of neuropsychological tests have been developed to measure various aspects of attention and have been included in research protocols evaluating the executive functions of children with ADHD. However, different researchers have applied different attentional constructs to these measures. Table 2 provides a listing of some of the more readily discussed attentional constructs and the tests used to measure them. Although it is common to make use of the construct interchangeably with the assessment device, researchers caution against this practice without clear knowledge of the requirements of the task and the specifications for the attentional construct based on a proposed model or results of factor analysis. As an example, Fletcher (1998) points out that cancellation tests have frequently been mislabeled as vigilance tasks. He notes that while vigilance tasks are specifically defined as those that require the subject to wait for increasingly longer periods of time for infrequently occurring events, cancellation tests provide the subject with a constant amount of information. Fletcher advances labeling cancellation

Table 2

Attention Component Labels Applied to Common Executive Function Measures

Measures	According to Mirsky's Model (1989)	According to Pennington & Ozonoff (1996)	According to Como (1997)
Continuous Performance Test	Sustain	Inhibition	Vigilance
Go/No-Go		Inhibition	
Letter Cancellation Test	Focus-execute		Vigilance
Matching Familiar Figures Test		Inhibition	Impulsivity
Paced Auditory Serial Addition			Focus
Porteus Maze Test		Planning	Impulsivity
Rapidly Recurring Figures Test			Focus, Selective, Sustain
Seashore Rhythm Test			Sustain, Vigilance
Speech Sounds Perception Test			Sustain, Vigilance
Stroop Interference Test	Focus-execute	Inhibition	Focus
Thurstone Word Fluency		Fluency	
Tower of London/Hanoi		Planning	
Trail-making Test, Parts (A &) B	Focus-execute	Set shifting	Divided, Focus, Impulsivity, Sustain
Underlining Test			Selective, Sustain
WISC-III Coding Subtest	Focus-execute		Sustain
WISC-III Digit Span Subtest	Encode	Working Memory	Vigilance
Wisconsin Card Sorting Test	Shift	Set Shifting	

tasks as measures of focused attention based on Mirsky's multifactorial model of attention. Based on a factor analysis of 10 frequently used measures of attention, Mirsky (1989) suggested that attention can be subdivided into four components: encode, focus-execute, sustain, and shift. He indicated that following: tests loading on the focus-execute component require ability to concentrate attentional resources to a specific task and to rapidly respond, tests loading on the sustain attention component require vigilance and an ability to inhibit unwanted responses, encode attention tasks require a mnemonic capacity

to hold information briefly and perform cognitive operations on it, and tests loading on the shift attention component require cognitive flexibility (Mirsky, Pascualvaca, Duncan & French, 1999).

One of the most common assessment devices used to measure sustained attention/vigilance is the continuous performance test (CPT). A continuous performance test requires the subject to continuously inhibit responding to frequent, though constantly changing, stimuli while remaining prepared to respond to infrequent target stimuli. A review of 30 years of research using various CPTs indicates that modifications across tests include visual vs. auditory stimuli, pictures vs. letters as visual stimuli, higher vs. lower frequency of target, longer vs. shorter stimulus duration, clear vs. degraded stimulus, and longer vs. shorter vs. variable interstimulus interval (Reynolds, Lowe, Moore, & Riccio, 1998). Conclusions based on the review suggest that CPTs are useful devices for screening for ADHD because of their high degree of sensitivity. In other words, most children with ADHD score poorly on CPTs. For example, studies that compared ADHD subjects to controls found both the number of omissions and number of commissions on the Gordon Diagnostic continuous performance test, in addition to number of correct responses, to be significantly different between the groups (Grodzinsky & Diamond, 1992; Mataro et al., 1997). However, results of the review also suggest that CPTs show low specificity and therefore are not useful in differentiating ADHD from other disorders involving CNS dysfunction. Contrary to the conclusions drawn by this review, CPT scores (number of omissions) have been shown to significantly differ between children with LD and children with ADD either with or without hyperactivity (Aylward et al., 1990; Barkley, Grodzinsky, & DuPaul, 1992). Furthermore, CPT scores

(number of commissions) significantly contributed to a discriminant function separating ADHD-only subjects from LD-only subjects from those with ADHD and LD (Robins, 1992). None of these studies excluded or evaluated for the effects of comorbid disruptive behavior disorders in the sample. While in some of the studies, children either had not begun psychostimulant medication treatment or discontinued taking any stimulant medication 48 hours before the assessment, a large percentage (68%) of children in other studies that found similar significant results were taking medications (Seidman, Biederman, Faraone, Weber, & Ouellete, 1997).

Other neuropsychological tests of executive function also appear to discriminate well between children with ADHD and normal controls. In particular, the Stroop test, a test of timed ability to inhibit prepotent responses in the presence of conflictual information (i.e., interference), appears to be sensitive to distinguishing between children with and without ADHD. In a brief review of the literature from 1986 to 1991, Barkley et al. (1992) found the results of five out of six studies consistent with the claim that the Stroop test differentiates between children with ADHD and controls. Similarly, more recent studies have consistently found control subjects to score significantly better than children with ADHD on both the first portion of the Stroop test requiring speeded reading of the names of colors and on the third, or interference, portion of the test (Barkley et al., 1992; Grodzinsky & Diamond, 1992; Seidman et al., 1997, Semrud-Clikeman et al., 2000). Results have been less consistent on the middle portion of the test requiring subjects to state the colors of series of x's as quickly as possible. In another study that found a significant group effect on the interference portion of the Stroop test, the results were further evaluated according to four age groups (7, 8, 9, and $\geq$ 10 years; Boucagnani

& Jones, 1989). No group by age interactions were found, suggesting that the effects of age on the Stroop are not different in the ADHD and control groups. Again, it can be noted that significant effects for the Stoop were found in children with ADHD both on and off stimulant medication. While research indicates that the Stroop test is sensitive to differences between children with ADHD and control children, it also appears to lack the specificity necessary to distinguish children with ADHD from children with other disorders such as LD (Barkley et al., 1992). This lack of specificity may in part be a function of the symptoms that represent a pathway for underlying behavioral problems manifested by several different diagnostic groups.

Children with ADHD are also reported to consistently perform more poorly than controls on measures of visuospatial planning (i.e., the Rey Osterrieth Complex Figure [ROCF]; Barr, Douglas, & Sananes, 1990; Grodzinsky & Diamond, 1992; Nigg et al., 1998; Seidman et al., 1995; Seidman et al., 1997). These significant group effects were found in studies that used the Waber and Holmes scoring procedure (Waber & Holmes, 1985). This scoring system assesses accuracy, level of organization, and style (i.e., part or configurational). Most often, children with ADHD showed deficient scores on assessment of organization. Studies that failed to find significant differences on the ROCF between children with and without ADHD failed to assess for organizational ability (Mataro et al., 1997; McGee, Williams, Moffitt, & Anderson, 1989). In support of the idea that stimulant medication may help improve organizational abilities, Barr et al. found that children with ADHD had improved ROCF copy scores when taking stimulants.

Numerous studies comparing the neuropsychological functioning of children diagnosed with ADHD versus normal controls use the Wisconsin Card Sorting Test (WCST) as a measure of executive functioning. The WCST has been referred to as a measure of shifting attention because of the requirement to overcome an established response set and shift set in response to examiner feedback. However, Barkley (1994) cautions against stating that the WCST represents a shift attention component because of the importance of other higher order cognitive processes (e.g., problem solving) that are also involved. Nonetheless, studies that assessed WCST variables such as failure to maintain set, trials to first category, and perseverative responses found significant differences between children with ADHD and controls (Boucugnani & Jones, 1989; Grodzinsky & Diamond, 1992; Seidman et al., 1997). Alternatively, studies that focused on the total number of categories completed failed to find significant differences (Mataro et al., 1997; McGee et al., 1989). The findings from measures of perseverative errors on the WCST yielded mixed results. These results are consistent with the review by Barkley et al (1992) indicating that significant deficits in children with ADHD relative to controls are found on measures of perseverative responses and perseverative errors.

Results from studies of the Controlled Oral Word Association test (COWA), a measure of phonemic verbal fluency, are also variable. A review of the literature indicates that some studies find deficits in verbal fluency in children with ADHD (Barkley et al., 1992; Grodzinsky & Diamond, 1992; Mataro et al., 1997) while others do not (Loge, Staton, & Beatty, 1990; McGee et al., 1989; Weyandt & Willis, 1994). The differential findings in the McGee et al. study may be due to the matching of reading ability and PIQ scores between the ADD subjects and controls. Because verbal fluency

scores have been shown to be related to reading ability, this matching may have eliminated a significant effect between ADHD subjects and normal controls. Though Loge et al. (1990) did not find reduced verbal fluency scores in the ADHD population, these children did commit significantly more rule violations, perhaps suggesting a failure to attend to the instructions or to inhibit inappropriate responses.

One test of executive functions which does not appear to discriminate well between ADHD subjects and normal controls is the Trail Making Test, part B. While this tests is a measure of flexibility based on a requirement to shift between two series, research consistently indicates that children with ADHD do not perform worse than controls (Barkley et al., 1992; Grodzinsky & Diamond, 1992; Mataro et al., 1997; McGee et al., 1989). Table 3 provides a summary of the findings on these executive functions in children with ADHD.

As indicated, the tests just reviewed are frequently used in research to evaluate children with ADHD because they are hypothesized to measure various aspects of attention. Furthermore, children with ADHD often show similar behaviors to frontal lobe lesion patients and these executive function tests have been shown to be sensitive to the effects of frontal lobe damage (Barkley et al., 1992; Boucugnani & Jones, 1989; Heilman, Voeller, & Nadeau, 1991). Lezak (1995) reviewed studies on each of these executive function tests and concluded that with each there appears to be a relationship between frontal lobe functioning and test performance. For instance, patients with left frontal lobe lesions are reported to show slowing on the interference trial of the Stroop test (Holst & Vilkki, 1988). Additionally, frontal damage is reported to increase a patient's perseveration and distortion of the ROCF. Research on patients with frontal

Table 3
Summary of Executive Functions Assessments in ADHD Versus Normal Controls

Authors, year of publication	CPT			Stroop			ROCF		WCST					COWA	TMT
	# correct	Comissions	Ommsiions	Word	Color	Interference	organization	accuracy	Trials to 1st Category	Failure to Maintain Set	# Categories	Perseverative Responses	Perseverative Errors	(FAS) # correct	Part B
Aylward et al., 1990	+	+													
Barkley et al., 1992		-	+	+	-	+	-		-	-	-	-	-	-	-
Boucagnani & Jones, 1989						+				-	+	+	+		+
Grodzinsky & Diamond, 1992	+	+	+	+	+	+			+	+	-	-	-	+	-
Loge et al., 1990	-	+							-	-	-	-	-	-	
Mataro et al., 1997	+	-	+			-		-			-	-		+	-
McGee et al., 1989								-	-				-	-	-
Seidman et al., 1997		-	+	+	+	+	+	-		-	+		+		
Weyandt & Willis, 1994												-		-	

Note. Numerous studies used executive function measures not listed in this table.
CPT = Continuous Performance Test
ROCF = Rey-Osterrieth Complex Figure;
WCST = Wisconsin Card Sorting Test
COWA = Controlled Oral Word Association;
TMT B = Trail Making Test, part B
+ = significant difference between ADHD and control children found
- = no significant difference found

lesions, and particularly dorsolateral prefrontal cortex damage, clearly indicates that they make more perseverative errors on the WCST (Grafman, Jonas, & Salazar, 1990). Results are less consistent with regard to whether these patients also achieve fewer categories. Although results suggest that the perseverative error score of the WCST is sensitive to frontal lobe lesions, research also suggests that patients with non-frontal lesions show impaired performance (Anderson, Damasio, Jones, & Tranel, 1991). Frontal lesion patients tend to have lower fluency scores on the COWA (Miceli, Caltagirone, & Gainotti, 1981). Though left-side lesion patients appear to do worse than right-side lesion patients on this test, both groups show deficits relative to controls. Finally, significant correlations have been reported between electrophysiological measures associated with frontothalamic functioning and the Trail Making Test (Segalowitz, Unsal, & Dywan, 1992).

Neuroimaging Findings

While deficiencies on tests of neuropsychological functioning in children with ADHD suggest specific neuroanatomical correlates to the disorder, numerous researchers have imaged the brains of children with ADHD in order to more accurately localize the anatomical substrates involved. Their research ultimately continues the search for support of Still's original hypothesis that ADHD results from a specific neurological deficiency. The results of a proliferation of both volumetric and metabolic studies beginning in the 1980's found reductions in the basal ganglia, cerebellum, and corpus callosum in addition to the frontal cortex (Castellanos, 1997).

Some of the pioneering studies implicating striatal dysfunction in ADHD were conducted by Hans Lou and colleagues in Copenhagen (Lou, Henriksen, & Bruhn, 1984;

Lou, Henriksen, Bruhn, Burner, & Nielsen, 1989). These early functional imaging studies, which were completed with xenon single-photon emission tomography (SPET), found low metabolic activity in the frontal white matter and basal ganglia of children diagnosed with ADD compared to a sibling control group. However, whether hypoperfusion was found in the caudate nuclei only, in the left and/or right striatum, or in other areas such as motor or primary auditory cortex varied across their studies. Some of the variation across studies may have been due to a failure to adequately specify diagnostic criteria and a failure to exclude subjects with comorbid diagnoses (e.g., dysphasia or mental retardation). These studies were also limited by the inclusion of ADHD subjects with other CNS complications (e.g., low neonatal oxygen levels), by partial volume effects from analyzing only a single thick axial slice, and by a failure to match controls for age and sex (factors suggested to be related to cerebral metabolism and blood flow).

The next wave of studies employed fluoro 2 deoxy D Glucose positron emission tomography (FDG PET) scans. Zametkin and colleagues (1990) began a five-year series of studies by assessing adults who were retrospectively diagnosed with ADHD and were also the parent of a child diagnosed with ADHD. Compared with controls who were matched for age, education and socio-economic status (SES), these ADHD subjects showed a lowered global cerebral glucose metabolic rate as well as decreased metabolism in the left frontal lobe in four specific regions of interest following control for overall metabolic rate. Follow-up studies in adolescents diagnosed with ADHD failed to find global metabolic rate changes but did find metabolic changes in both the left frontal, left thalamus, and right temporal lobes (Zametkin et al., 1993). Subsequent studies which

assessed the effects of acute or chronic stimulant treatment in adults with ADHD (using dextroamphetamine or methylpenhidate, i.e., Ritalin) also failed to find global glucose metabolism changes (Matochik et al., 1994; Matochik, Nordahl, Gross, &, 1993). However, these studies did find a variety of positive results that were dependent upon the particular stimulant medication taken as well as chronicity of treatment. The significant results included increased metabolic rates in the right caudate, right thalamus, left or right frontal cortex, and right temporal cortex as well as decreased metabolic rates in left or right frontal cortex, left parietal cortex, and basal ganglia.

Each of these FDG PET studies were limited by problems common to PET scan research, including an inability to quantify small regions due to poor spatial resolution and poor temporal resolution secondary to averaging metabolic activity over approximately 40 minutes. Furthermore, these studies failed to correct statistically for multiple comparisons. Therefore, some of the significant changes in metabolic rate may have simply been due to chance results of conducting numerous t-tests.

Contemporaneous with these functional imaging studies, studies using magnetic resonance imaging (MRI) to assess global and regional brain volume were being completed to further our understanding of the neuroanatomy of subjects with ADHD. Though early MRI studies were plagued by use of small sample sizes and 0.6 T scanners providing thick image sections, these studies showed preliminary support for the hypothesis that ADHD is a disorder of abnormal prefrontal structure/circuitry (Hynd, Semrud-Clikeman, Lorys, Novey, & Eliopulos, 1990; Hynd et al., 1993). Hynd and colleagues failed to find a significant main effect for group when comparing ADHD subjects with dyslexic subjects or normal control subjects; however, an interaction effect

indicated that ADHD subjects show decreased size of the left caudate compared to normal control subjects. It is noteworthy, however, that children diagnosed with ADHD were also diagnosed with a significant number of other diagnoses, including CD, ODD, dysthymia, and developmental arithmetic disorder. In a more recent study comparing a clean ADHD population (i.e., no comorbid learning disability, psychiatric diagnosis, or significant medical history) with normal controls, reversed caudate asymmetry was found in the ADHD population (Semrud-Clikeman et al., 2000). Additionally, greater reversal of asymmetry was associated with poorer scores a Stroop test and a greater incidence of loss of set on the WCST.

Multiple MRI studies were also conducted specifically to assess for differences in the corpus callosum of ADHD subjects and normal controls. While the overall shape and size of the corpus callosum in ADHD subjects was not judged to differ significantly from control subjects, individual regions of the corpus callosum were decreased in size (Giedd et al., 1994; Semrud-Clikeman et al., 1994; Baumgardner et al., 1996). Unfortunately, whether the rostrum, body, or splenium of the corpus callosum in ADHD subjects was found to be smaller relative to control subjects depended on the study reviewed.

A series of studies conducted by Castellanos and colleagues addressed many of the weaknesses of previous studies and ultimately implicated right frontal-striatal circuitry in ADHD (Casey et al., 1997; Castellanos et al., 1994; Castellanos et al., 1996). Castellanos and colleagues achieved a large sample of children meeting DSM-III-R criteria for ADHD according to a diagnostic interview and/or the Conners' parent and teacher rating scales. These subjects were compared to a large sample of control subjects matched for age, height and weight, pubertal stage, and handedness. Strong exclusion

criteria were implemented, including IQ < 80, presence of Tourrette's syndrome, or the presence of any Axis I psychiatric diagnoses (other than CD or ODD). They assessed the volumes of multiple brain regions using a 1.5 T scanner providing contiguous 2 mm sections. All volumetric assessments were completed by blind raters who achieved interrater reliability scores $\geq$ .82. Furthermore, all behavioral measures on the subjects were completed off medications in order to enhance any differential abilities of control children vs. children with ADHD.

In many of the studies in this series, lowered total cerebral volume was found for children with ADHD compared to controls. However, covarying IQ often eliminated this effect. Other significant findings included significantly lower right anterior frontal, right caudate, and right globus pallidus volumes in ADHD children compared to control subjects. These findings are consistent with the definition of ADHD proposed by Zametkin et al. (1993) that ADHD results from a disruption of subcortical pathways related to the regulation of arousal and motor inhibition that manifests as deficits in attention, impulse control, and motor activity. Interestingly, Mataro et al. (1997) also concluded that dysfunction in ADHD can be attributed to the right caudate nucleus. However, their results showed that the volume of the right caudate nucleus was enlarged in comparison to normal controls.

Multiple studies using MRI techniques to assess volumetric discrepancies between children diagnosed with ADHD and normal control subjects also found decreased volume in the cerebellum of children with ADHD (Berquin et al., 1998; Castellanos et al., 1996; Mostofsy, Reiss, Lockhart, & Denckla, 1998). Castellanos and colleagues found that right globus pallidus volume, caudate symmetry, and left cerebellar

volume together correctly classified 78% of the ADHD subjects and 65% of the control subjects in a step-wise discriminant function analysis. Cerebellar volume in this study was defined as the sum of vermian lobules I-V, VI-VII, and VIII-X and did not include hemispheric measurements. Three other studies found cerebellar volume to be significantly reduced in the vermal region. (Berquin et al., 1998; Castellanos et al., 2001; Mostofsky et al., 1998). In the two earlier studies, the posterior inferior lobe (lobules VIII-X) in particular was noted to be involved in the reduction in males with ADHD. Mostofsky and colleagues found significant differences between ADHD and control subjects on measurements of the ratio of the posterior vermis to total intracranial volume. Castellanos and colleagues found similar results in a cohort of females with ADHD. Generally, these results are consistent with one of the earliest neuroimaging studies in an ADHD population which showed that 25% of the subjects diagnosed with hyperkinesis/minimal brain dysfunction showed cerebellar atrophy compared to only one control subject (Nasrallah, Loney, & Olson, 1986).

The most recent studies of neuroimaging in ADHD utilized fMRI techniques. The recency of most of these studies dictates that ADHD diagnoses were made according to DSM-IV criteria. A consistent finding from these studies appears to be the effect of methylphenidate on basal ganglia activation. For example, Vaidya et al. (1998) found methylphenidate to increase striatal and frontal activation in children with ADHD. The hypothesis of right frontal-striatal circuitry dysfunction in ADHD was also supported in an fMRI study that found a correlation between the right caudate size and activation during a continuous performance task (CPT) in an ADHD population (Teicher, Polcari, & Anderson, 1996). In a more recent study assessing response inhibition, Bush and

colleagues found hypoactivation of the anterior cingulate (cognitive division) in subjects diagnosed with ADHD. Together, these studies suggest impairment in a fronto-striatal attention network in ADHD subjects.

While the studies to date suggest that dysfunction in ADHD may be attributed to decreased volume or metabolic activation in the basal ganglia, cerebellum, corpus callosum, or frontal cortex, the specific results remain inconclusive because of variable finding across studies. Table 4 provides a summary of the neuroanatomical abnormalities found in ADHD subjects. For example, though decreased volume or activation in the basal ganglia was suggested, results conflict with regard to whether this volumetric decrease or metabolic reduction occurs in the left versus right caudate, the left versus right globus pallidus, or more generally in the left versus right striatum. Furthermore, some studies, which only reported cerebellar abnormalities in the vermis did not indicate that null results were found in other regions of the cerebellum. Rather, they noted that other regions of the cerebellum were not easily quantifiable (Ciesielski, et al, 1997). Similarly, many studies failed to assess for cerebellar abnormalities, thereby suggesting that a failure to find cerebellar abnormalities in ADHD may result from a failure to measure the cerebellum rather than negative findings (Aylward et al., 1996). This point is highlighted in a recent review of neuroimaging studies in ADHD where it is stated that structural imaging studies show smaller prefrontal and caudate volumes in ADHD and functional imaging studies reveal hypoperfusion or hypometabolism in these same regions. While these findings are real, the reviewers failed to include structural imaging studies assessing cerebellar size or activity. Additionally, functional imaging studies of the cerebellum in an ADHD population have not been completed to date.

Table 4
Summary of Positive Neuroimaging Findings in ADHD Versus Control Subjects

First Author, year of publication	Imaging technique	Number of ADHD & controls	Findings in ADHD
Significant findings in the **Cerebellum**:			
Berquin et al., 1998	MRI	46 47	↓ Vermis of Cerebellum
Castellanos et al., 1996	MRI	57 55	↓ Cerebellum
Castellanos et al., 2001	MRI	50 50	↓ Posterior-Inferior Vermis (lobules VIII-X) of Cerebellum
Mostofsky et al., 1998	MRI	12 23	↓ Posterior-Inferior Vermis (lobules VIII-X) of Cerebellum
Significant findings in the **Basal Ganglia**			
Aylward et al., 1996	MRI	10 11	↓ L Globus Pallidus
Castellanos et al., 1994	MRI	50 48	Lack of normal R > L Caudate asymmetry
Castellanos et al., 1996	MRI	57 55	↓ L and R Globus Pallidus Lack of normal R > L Caudate asymmetry
Filipek et al., 1997	MRI	15 15	↓ L Caudate Reversal of normal R > L Caudate asymmetry
Hynd et al., 1993	MRI	11 11	↓ L Caudate Reversal of normal R > L Caudate asymmetry
Lou et al., 1984	Xenon emission CT	11 9	Hypoperfusion in R and L Caudate
Lou et al., 1989	Xenon emission CT	19 9	Hypoperfusion in R and L Striatum
Mataro et al., 1997	MRI	11 19	↑ R Caudate
Vaidya et al., 1998	fMRI	10 6	Hypoperfusion in Striatum

Table 4 - continued

Authors, year of publication	Imaging technique	Number of ADHD & Controls	Findings in ADHD
Significant findings in the **Frontal Lobes**:			
Bush et al., 1999	fMRI	8 8	Hypoactivity in the Anterior Cingulate (cognitive division)
Castellanos et al., 1996	MRI	57 55	↓ R Frontal region
Filipek et al., 1997	MRI	15 15	↓ R anterior-superior Frontal region ↓ R and L anterior-inferior Frontal region
Hynd et al., 1990	MRI	10 10	↓ R anterior region
Lou et al., 1984	Xenon emission CT	11 9	Hypoperfusion in R and L Frontal region
Vaidya et al., 1998	fMRI	10 6	Hypermetabolism in Frontal regions during task
Zametkin et al., 1993	PET	10 10	Hypoperfusion in L anterior and posterior Frontal regions
Significant finding in other **Cortical Regions**:			
Lou et al., 1989	Xenon emission CT	19 9	Hypoperfusion in L Sensorimotor and Occipital regions
Zametkin et al., 1993	PET	10 10	Hypoperfusion in R Temporal region
Significant finding in the **Corpus Callosum**:			
Baumgardner et al., 1996	MRI	13 27	↓ Rostral Body of Corpus Callosum
Giedd et al., 1994	MRI	18 18	↓ Rostrum and Rostal Body of Corpus Callosum,
Semrud-Clikeman et al., 1994	MRI	15 15	↓ Posterior Corpus Callosum (Splenium)

Note. Some studies appear in the table more than one time.
L = Left, R = Right

Neurological Soft Signs

Further support for the idea that ADHD symptomotology is due to neurological dysfunction comes from studies that assess neurological "soft signs" in this population. Soft neurological signs comprise a heterogeneous group of nonfocal neurological abnormalities involving both motor and sensory performance (Vitiello, Stoff, Atkins, & Mahoney, 1990). Research on the reliability of soft signs indicates that some of the more reliable signs include nystagmus, dyspraxia of tongue movements, and simultanagnosia (i.e., inability to recognize a scene with preserved recognition of elements of the scene; Spreen, Risser, & Edgell, 1995). Early research of hyperactive children found soft neurological signs to be more common in this population than in controls (Denckla & Rudel, 1978; Mikkelsen, Brown, Minichiello, Millican, & Rapoport, 1982; Werry et al., 1972). Using a discriminant function analysis, Denckla and Rudel found that measurement of nine soft sign variables produced a significant discrimination between boys diagnosed with hyperactivity and normal controls and correctly classified 89% of the children. Incorrect classification generally resulted from false negatives (failure to diagnose ADHD) rather than false positives. The variables which contributed to correct classification of the boys included motor overflow (synkinesis and mirror movements), heel-toe and pronation-supination (both measures of rapid alternating coordination/dysrhythmia), toe taps, hand pats, finger pats, and finger-to-thumb successive movements. Many of these tests have been described as basic tests of coordination or cerebellar function (Mayo Clinic, 1976). A more recent study also noted a significant incidence of soft neurological signs in children with ADHD, though they indicated that these soft signs were specifically related to sensory defensiveness

(Foodman & McPhillips, 1996). In their study evaluating children with ADHD, CD, or ODD and normal controls, Vitiello and colleagues found that performance on a measure of soft signs (the total score from the Revised Neurological Examination for Subtle Signs) was positively correlated with performance on executive function measures (e.g., a continuous performance test). In another study assessing both neuropsychological and neurological findings in children diagnosed with ADHD, results suggested that these children showed more right-sided and overall soft signs than non-ADHD children (Aronowitz et al., 1994). These children also had reduced scores on tests of organization and problem solving (e.g., WCST, Neimark Memorization Strategies Test). These research findings suggest that in an ADHD population, the degree of soft neurological signs exhibited by the child relates to his/her degree of executive dysfunction.

Eye Movement Problems

As indicated, general assessments of soft neurological signs often include assessments of eye movements. However, individual studies of soft signs in children with ADHD often fail to indicate whether the evidence for soft signs specifically included observations of abnormal eye movements. Alternatively, studies have been conducted which have directly assessed oculomotor control in children with ADHD. Many of these studies used a Posner paradigm where the subject is cued as to where he or she will eventually shift gaze but must delay for a short period before shifting gaze to the previously cued location. These types of tasks have also been referred to as visual-spatial cueing tasks or oculomotor delayed response tasks and they purport to measure memory-guided saccades (Ross, Hommer, Breiger, Varley, & Radant, 1994; Swanson et al., 1991). Saccades are rapid eye movements made to redirect the focal line of sight.

Research suggests that memory-guided saccades are controlled by the dorsolateral prefrontal cortex (DLPFC) due to the working-memory component of encoding the location of a target until an appropriate saccade can be made (Kori, Das, Zivotofsky, & Leigh, 1998). Findings indicate that ADHD subjects show a higher percentage of trials with premature saccades than control subjects, further implicating the DLPFC in ADHD dysfunction. The ADHD subjects' failure to inhibit responding until the cue disappeared occurred both ipsilateral and contralateral to the cued stimuli, while normal controls did not show an inhibition deficit. Interestingly, this type of inhibition was not attenuated by the effects of methylphenidate, a common stimulant medication used to control behavioral inhibition problems (Ross et al., 1994; Quay, 1997).

While these studies utilized memory-guided saccadic eye movements tasks, these tasks were employed as a measure of cognitive functioning, namely inhibition, rather than as a measure of neurological control of eye movements. However, it has been reported that many children with ADHD show deficient smooth pursuit capabilities (B. Maria, M.D., personal communication, June, 1999). Smooth pursuit is the ability to visually track a target without evidence of nystagmus or saccades. A review of the literature indicated that only one series of studies directly evaluated smooth pursuit as well as anticipatory saccadic eye movements in an ADHD population (Jacobsen et al., 1996). Rate of smooth pursuit, or gain, is defined as eye velocity divided by target velocity. Anticipatory saccades are saccades in the direction of the target motion that increase position error. This type of saccade is controlled by the cerebellum. (Saccades in the direction of target motion that decrease target error are referred to as catch-up saccades). Jacobsen and colleagues found that ADHD subjects scored significantly lower

than normal controls (and higher than schizophrenic subjects) on a global measure of time spent in smooth pursuit tracking of a target. Although on the remainder of measurements (e.g., smooth pursuit gain or mean saccadic frequency) ADHD subjects did not score significantly different from controls, their scores were consistently lower than those of controls. As research in this area is limited, further study into the eye movement capabilities of children with ADHD is necessary before conclusions can be drawn.

Neuroanatomical Substrates

Currently, the literature reviewed on neuroimaging or neurological evaluations of ADHD subjects suggests a variety of neuroanatomical regions may be involved in the dysfunction found on assessment. While research findings from neuroimaging studies suggest that neuroanatomical abnormalities in ADHD subjects exist in frontal, basal ganglia, and/or cerebellar areas, neuropsychological assessments have nonetheless frequently only focused on evaluating behaviors analogous to frontal lobe functions. As indicated, this focus emerged following findings of similarities in symptomotology between frontal lobe lesion patients and ADHD patients (Barkley, et al, 1992; Boucugnani & Jones, 1989). Alternatively, researchers have hypothesized about the involvement of the basal ganglia and cerebellum in addition to the frontal lobes in ADHD dysfunction. In her review of the networks involved in developmental disabilities (including ADHD), Denckla (1998) noted that ADHD has been described as belonging to a diagnostic group labeled "developmental disorders of the basal ganglia." She indicated that there is strong evidence for basal ganglia dysfunction in ADHD. While she advocated the importance of continued neuroimaging of the frontal component of the

frontal-subcortical loop purported to be involved in ADHD, she nonetheless, also focused on the need to further elucidate the role of the subcortical component through neuropsychological testing paradigms. It is important to note that in this review, subcortical is defined as including the cerebellum in addition to the basal ganglia. In support of her call furthering our understanding of the subcortical component of ADHD, Denckla summarized the results of research which showed that ADHD is associated with motor slowing, poor response preparation, and subtle neurological motor control signs (e.g., overflow movements indicative of motor disinhibition) each suggestive of "subcortical" involvement.

In conjunction with Denckla's theory, other researchers have hypothesized about the role that frontal cortex, basal ganglia structures, and the cerebellum may play in ADHD. For example, Voeller and Heilman (1988) suggested that impairment in ADHD may be secondary to brainstem (i.e., pons, cerebellum, or medulla) and/or diencephalic (i.e., thalamic, epithalamic, hypothalamic, or subthalamic) dysfunction. Specifically, they found that children with ADD omitted over twice as many letters as control subjects on a letter cancellation task. Furthermore, these errors were concentrated on the left side of the page for the ADD participants. These results, taken together with findings of predominantly left-sided subtle neurological signs in the ADD subjects, were interpreted as evidence of right hemisphere cortical, brainstem, or diencephalic dysfunction in ADHD.

The developmental chronometry hypothesis, proposed by Ciesielski, Harris, Hart, and Pabst (1997) also lends support to the hypothesis that abnormalities in children with ADHD may exist within a frontal-subcortical-cerebellar system in ADHD. According to

this hypothesis, abnormalities in cerebellar and frontal subsystems likely result in similar deficits in a variety of developmental disorders. The key feature of this developmental hypothesis is that areas such as the cerebellum and frontal lobes are both late maturing areas of the brain. Ciesielski et al. (1997) cite phylogenetic and ontogenetic evidence for this protracted course of development. Phylogenetically, the neocerebellum and prefrontal brain regions have evolved in parallel in hominids. Ontogenetically, both the cerebellum (specifically the posterior neocerebellum) and the prefrontal cortex have a slow and prolonged courses of development through the first two or three decades of a persons life. Due to this prolonged course of postnatal development, these areas are particularly vulnerable to early insult. Therefore, according to the developmental chronometry hypothesis, both the cerebellum and prefrontal cortex subsequently become common sites of structural or functional abnormalities in developmental disorders.

Beyond phylogenetic or ontogentic relation, there is further evidence that specific pathways connect the frontal lobes and the cerebellum. As will be discussed in the following section, it has been suggested that the cerebellum may function to modulate higher cognitive functions (Schmahmann, 1991). Part of the neuroanatomy hypothesized to underlie this modulation is the corticopontocerebellar pathway. The cortical areas involved in this pathway include the frontal, parietal, and temporal lobes. Connections to the pons from the frontal lobes extend from association areas of the prefrontal cortex as well as from primary and supplementary motor areas. Schmahmann suggests that the feedback component of this pathway would extend from the neocerebellar region (in particular, the dentate nucleus) through the dorsal medial, ventrolateral, or intralaminar nuclei of the thalamus into the prefrontal cortex. While Schmahmann did not

hypothesize specifically about the impact on ADHD from dysfunction in this loop, it does encompass many of the structures found to be abnormal, either structurally or functionally, in ADHD population.

Further evidence in support of subcortical-cerebellar involvement in ADHD comes from research on the effects of a common psychostimulant on regional brain glucose metabolism (Volkow et al., 1997). Among 15 healthy adult male subjects, the effects of two sequential intravenous doses of methylphenidate were variable. It significantly increased regional brain metabolism in six subjects, decreased metabolism in two, and did not have effect on metabolism in the remaining seven. However, methylphenidate consistently increased metabolism in the cerebellum across all subjects while decreasing relative metabolic activity in the basal ganglia. Furthermore, the metabolic changes in the frontal lobes and cerebellum were associated with measures of dopamine receptor availability. In other words, the effects of methylphenidate on brain activity depended in part on the state of the dopamine system. This finding is consistent with the findings that methylphenidate decreases behavioral activity in children with ADHD but is reported to increase restlessness in normal controls. Volkow et al. conclude that although there are almost no dopamine receptors in the cerebellum, methylphenidate might be effective through the striatal projections into the cerebellum.

The Cerebellum

Neuroanatomy

In order to better understand how the cerebellum may be involved in the deficits seen in children with ADHD, a review of the neuroanatomy of the cerebellum is necessary. The human cerebellum is the most densely populated area of the brain with

the number of nerve cells reported to exceed the number in the cerebral cortex (Leiner, Leiner & Dow, 1991). Furthermore, there are approximately 20 million nerve fibers projecting into the cerebellum via the pons from the cortex. Though the cerebellum currently accounts for a significant portion of brain mass, phylogenetic information reveals that spanning hominid development, the cerebellum underwent a three to fourfold increase in size (Leiner, Leiner & Dow, 1986). The phylogenetically newest parts of the cerebellum not only developed in parallel with the cerebral cortex generally, but more specifically evolution of the neocerebellum paralleled development of cerebral association areas. Evolution of the dentate nucleus within the neocerebellum also evidenced this unproportional enlargement. Not only is the human dentate nucleus significantly larger than the other three cerebellar nuclei, but also the dentate in humans exceeds its size in other species.

Ontogentic development of the cerebellum within humans recapitulates phylogentic development of the cerebellum. More specifically, the cerebellum is one of the last structures to mature in the human brain and does so concomittantly with the frontal lobes.

Structurally, the cerebellum consists of cortical gray matter, a white matter core consisting of three peduncles, and four pairs of deep cerebellar nuclei: fastigial, globus, emboliform, dentate. The globus and emboliform are commonly referred to together as the interpositus nuclei. The body of the cerebellum can be divided into lobules according to deep folia also known as fissures. However, most often researches refer to the three functional divisions of the cerebellum: vestibulocerebellum, spinocerebellum, and

cerebrocerebellum (Kingsly, 1996). These three divisions are based on connections made to the surrounding nervous system.

The vestibulocerebellum, also known as the archicerebellum, is comprised primarily of the flocculonodular lobe. It receives the majority of its afferent (feedforward) fibers from the vestibular nuclei by way of the inferior cerebellar peduncle. Axons (of Purkinje cells) exit the vestibulocerebellum after synapsing in the associated deep cerebellar nucleus, namely the fastigial nucleus. From there, efferent (feedback) fibers travel through the contralateral inferior cerebellar peduncle to the vestibular nuclei and reticular formation. The vestibulocerebellum primarily regulates gait and posture by coordinating head, eye, and body movements. Lesions to this region result in staggering, ataxic gait, nystagmus and vertigo.

The spinocerebellum (paleocerebellum) includes the vermis and a thin strip of the medial hemishperes adjacent to the vermis, referred to as the intermediate hemisphere. The vermis can be further subdivided into nine regions. The anterior vermis consists of lobules I – IV, the central lobule and culmen. The primary fissure divides the anterior vermis from the superior-posterior vermis. This region of the vermis encompasses lobules VI-VII, the declive, folium, and tuber. Finally, the prepyramidal fissure divides the superior-posterior vermis from the inferior-posterior vermis (lobules VIII-IX, pyramis and uvula, respectively). The spinocerebellum receives its primary input from the spinal cord through two fiber tracts known as the dorsal and ventral spinocerebellar tracts. Purkinje cells of the spinocerebellum synapse in the fastigial nuclei and interpositus nuclei (globus plus emboliform nuclei). As indicated, axons leaving the fastigial nucleus do so through the inferior cerebellar peduncle. Alternatively, axons from the

interpositus nucleus exit the cerebellum through the superior cerebellar peduncle and terminate in the contralateral red nucleus or thalamus. The spinocerebellum is primarily responsible for proprioception and axial limb placement.

The third functional division of the cerebellum is referred to as the cerebrocerebellum. This phylo- and ontogenetically most recent part of the cerebellum to develop is, therefore, also referred to as the neocerebellum. It consists of the remainder of the cerebellar hemispheres. This region primarily receives its input from the contralateral pontine nuclei. As mentioned, approximately 20 million axons from all four lobes of the cerebral cortex project to the contralateral pontine nuclei and then enter the cerebellum through the middle cerebellar peduncles. Projections from the frontal lobes also reach the neocerebellum through the red nucleus and inferior olive. Axons of purkinje cells leaving the cerebrocerebellum first project to the dentate nucleus. They then pass through the superior cerebellar peduncle to terminate in the contralateral thamalus similar to the interpositus projections.

Cerebellar output channels are directed to a variety of cortical areas including primary motor, premotor, oculomotor and prefrontal cortex (see Figure 1). They also project through a variety of thalamic nuclei in addition to the classic motor thalamic nuclei (Schmahmann & Pandya, 1997).

Research suggests that the cerebellar outputs arise from distinct areas of cerebellar nuclei before projecting to distinct areas within cortical regions. Middleton & Strick (1997) conducted a series of studies to support this hypothesis using transneuronal transport of the herpes simplex virus in primates. This virus tracing technique revealed that there is a feedback system from the caudal portion of the anterior dentate and

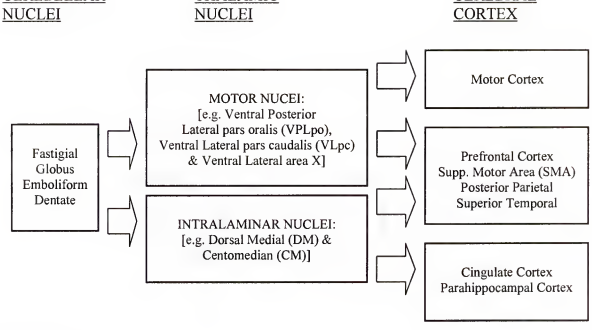


Figure 1.
Cerebellar Projections

interpositus nuclei through the ventral lateral and ventral posterior lateral nuclei of the thalamus to the primary motor cortex of the cerebrum. Using the same technique, projections from the most caudal region of the dentate to the frontal eye fields (underlying voluntary eye movements) were also observed.

While it has long been accepted that the cerebellum is involved in the control of motor behavior, only recently has research begun to support the idea that the cerebellum may similarly be involved in the control of higher cortical functions (Leiner et al., 1991, Middleton & Strick, 1997). In order to better understand the feedback projections from cerebellar nuclei to non-motor regions of the cerebral cortex, Middleton & Strick (1994) again used retrograde transneuronal transport of the herpes simplex virus type 1. They chose to evaluate the innervation of the dorsolateral prefrontal cortex (DLPFC) because of its characterization as a non-motor region of the frontal lobes. More specifically, this

region of the frontal lobes is thought to play an essential role in the integration of higher cognitive functions such as working memory, planning, language and attention (Schmahmann & Pandya, 1997). During this procedure, the herpes virus was injected into the DLPFC and retrograde labeling was seen in three thalamic nuclei: ventral anterior, ventral lateral, and dorsal medial. Retrograde labeling was also observed in the dentate nucleus of the neocerebellum, and particularly within the most ventral portion of the nuclei contralateral to the injection site. Thus, they concluded that there are distinct targets within the cerebello-thalamo-cortical connections and the pathway from the ventral dentate through the thalamus to the DLPFC is distinct from those innervating motor cortex. They go on to suggest that the output from these parts of the cerebellum and basal ganglia to the DLPFC project back to the basal ganglia, thereby creating a closed loop. The anatomic link between the DLPFC and the cerebellum provides critical support for the hypothesis that the cerebellum may contribute to cognition (Schmahmann & Pandya, 1997).

Cognitive Correlates

While still a relatively new concept, numerous researchers have begun to evaluate the role of the cerebellum in higher cognitive functions. The primary cognitive processes focused on in the literature are those which functionally link the cerebellum, basal ganglia, and frontal lobes (Leiner et al., 1986). Therefore, the cerebellum has been found to contribute to cognitive skills such as verbal fluency, associative learning, anticipatory planning/use of cues, and attention.

The anatomy of the cerebro-cerebellar system, in particular connections between the neocerebellum and the prefrontal cortex, suggests that the cerebellum can contribute

to the learning of cognitive/language skills in addition to motor skills (Leiner, Leiner, & Dow, 1993a). Research on patients with cerebellar damage supports this hypothesis. For instance, a case study of a 20 year-old male patient with extensive sulcal widening and volume loss in the cerebellum revealed frontal/executive and language deficits in addition to numerous neurological signs commonly associated with cerebellar abnormalities (Akshoomoff, Courchesene, Press, & Iragui, 1992). The neurological signs included vertical nystagmus, impaired smooth pursuit eye movements, intention tremor, head titubation (i.e., tremor or shaking), dysarthria (i.e., incoordination of the muscles for speech), ataxia (i.e., impaired ability to coordinate muscles during voluntary movement), dysmetria (i.e., impaired ability to control the distance, power, and speed of an action), and dysdiadochokinesia (i.e., impaired ability to perform rapid alternating movements). A review of his neuropsychological test results indicated that his most significant deficit was in the area of verbal fluency, though deficits in naming, associative and verbal learning were also apparent. This patient's verbal fluency deficit (in light of fluent, syntactically normal, speech) is consistent with research findings of activation in the inferior lateral cerebellum in healthy controls during a semantic association task (Petersen, Fox, Posner, Mintun, & Raichle, 1989). During this task, performed during PET scanning, activation in the right neocerebellum occurred when control subjects were required to state appropriate verbs for nouns presented. This activation differed from the medial cerebellar activation associated with simple verb generation or noun repetition likely due to the basic motor component of speech. In contrast to the verbal fluency deficits seen in the case study, the patient scored within the average to low average range on measures of receptive vocabulary, verbal memory, visuoperceptual functions, and

problem solving. It is noteworthy that this patient was reported to be unimpaired on a measure of problem solving because of his normal score on the WCST categories achieved. However, he did fail to maintain set three times, a moderately impaired score and indicative of difficulty with sustained attention and/or impulse control.

In a follow up to the PET study on normal controls which found activation in the cerebellum during a semantic association task, Fiez, Petersen, Cheney and Raichle (1992) evaluated a patient with right neocerebellar damage who showed above average performance on intelligence and memory measures. They consistently found two types of results on word association tasks when comparing the patient to a group of three male controls matched for age, education, and intelligence. First, they found a large number of incorrect and/or atypical associative words generated. Additionally, they found a lack of improvement in reaction time with practice. Essentially, this patient failed to show the normal ability to learn associations.

Research studies have also compared the functioning of groups of patients with cerebellar lesions to normal controls on measures of associative and other non-motor learning paradigms (Bracke-Tolkmitt et al., 1989). In their study, Bracke-Tolkmitt et al. evaluated five patients with cerebellar lesions ranging from an excised left cerebellar astrocytoma to olivo-ponto-cerebellar atrophy. Again, neurological signs consistent with cerebellar damage such as saccadic smooth pursuit, nystagmus, ataxia, dysarthria, and intention tremor were evident in various combinations in each of the patients. The patients were impaired on two measures of associative learning. They were not impaired on a number of other neuropscyhological measures (e.g., memory for stories, visuospatial copy or recall, and digit span).

While the previous studies suggest that the cerebellum plays a role in associative learning, this finding was not supported in another study of 12 patients with cerebellar lesions (Helmuth, Ivry, & Shimizu, 1997). These patients were not impaired versus controls on generating rule-based semantic associations. These discrepant findings suggest that conclusions about the role of the cerebellum in associative learning remain equivocal.

A person's ability to use cues to improve their performance is evidence of anticipatory planning abilities. On reaction time tasks, healthy subjects normally show a strong effect for valid cues versus invalid cues (Leiner et al., 1986). In other words, their response times are significantly faster when they are correctly cued because they are able to plan their response. Alternatively, results from a patient with right unilateral cerebellar damage secondary to occlusion of the posterior inferior cerebellar artery indicate that cerebellar damage may preclude ability to make use of cues for anticipatory planning (Leiner et al., 1986).

Cognitive planning abilities were further evaluated in nine patients diagnosed with pure cerebellar cortical atrophy (Grafman et al., 1992). Although the cause of the cerebellar atrophy was not indicated, it was noted that these patients did not show atrophy extending into the pontine area. Results of an ANOVA comparing the patients with cerebellar atrophy to normal controls indicated that the patients solved significantly fewer problems using the Tower of Hanoi task. Furthermore, the patients made significantly more "illegal" moves (i.e., moves that break the rules established at the outset of the task). Finally, between group analyses revealed that the patients took a significantly longer amount of time to plan for their first move when compared to the controls.

Grafman et al. (1992) hypothesized that patients with frontal lobe damage and cerebellar damage show similar deficits on planning tasks such as the Tower of Hanoi because the frontal lobes and cerebellum have complimentary roles in executing such tasks. They suggest that the frontal lobes are responsible for the initiation of plans or cognitive sequences while the cerebellum coordinates on-line temporal integration of the actions making up the cognitive plan.

Another cognitive dysfunction that has been associated with cerebellar damage and supports the hypothesis of a functional link between the cerbellum, basal ganglia, and frontal lobes is inattention. In a study of attention in rats, Anderson (1994) found that attention to novelty was strongly associated with total cerebellar volume. More specifically, it was found that a greater volume of the molecular layer, which is composed of Purkinje cell dendrites, was associated with an increased tendency to attend to novel stimuli. The author concluded that a deficient number of cerebellar connections is predictive of problems with inattention.

A functional imaging study of six healthy normal control subjects also revealed that the cerebellum is likely involved in attention (Allen, Buxton, Wong, & Courchesne, 1997). In this study, the subjects were imaged while completing a task that required selective attention to specific shapes or colors. The activation during this task was compared to activation during a motor task requiring the subjects to make paced movements with their right hand. Results indicated that not only was the cerebellum activated during both the attention and motor tasks, but also these two tasks activated independent volumes within the cerebellum. Though these tasks differentially engaged volumes within the cerebellum, it is notable that at the onset of the motor task, there was

a brief activation in the area of the cerebellum associated with attention. According to Allen et al. these findings indicate that one of the primary functions of the cerebellum is to respond during the early stages of learning, whether motor or non-motor.

Shifting attention deficits have also been associated with cerebellar damage. Results from a series of studies on patients with neocerebellar damage suggest that ability to shift attention either between or within modalities is controlled, at least in part, by the cerebellum (Akshoomoff & Courchesne, 1992; Akshoomoff & Courchesne, 1994; Courchesne et al., 1994). These studies are discussed in more detail below.

While the previous studies focus on specific roles for the cerebellum (e.g., verbal fluency or planning), the cerebellum has also been conceptualized as a more general control center, controlling motor movements and/or manipulation of symbols (i.e., cognitive functions; Leiner, Leiner, & Dow, 1993b). The involvement of the cerebellum in the manipulation of symbols may be conceptualized as a precursor to the processes of intention and attention. Referring to a function of the DLPFC, Heilman, Valenstein, and Watson (1997) described intention as a triage process whereby action is prepared for. They also described attention as a triage process where stimuli are routed for processing based on judgements of novelty and importance. The conclusions that patients with cerebellar damage show deficits in anticipatory planning, use of cues, problems solving, and verbal fluency suggests intentional control deficits by these patients. Similarly, deficits in attention to novelty, selective attention, and shifting attention suggests attentional control deficits in cerebellar lesion patients.

Further support for the idea that the cerebellum plays a role in mediating cognitive functions comes from a review of the literature on developmental disabilities

with associated cerebellar abnormalities. For example, Ciesielski et al. (1997) used MRI techniques to measure the cerebellums of 11 children with autism, 10 survivors of acute lymphoblastic leukemia, and 10 normal controls. They also evaluated each of the children/adolescents on a battery of neuropsychological tests. While the researchers reported inability to measure the hemispheres of the cerebellums because of high inter-rater variability, they found significant differences in vermal measurements between the normal controls and the subjects with disorders of childhood. Furthermore, they concluded that the most distinct cognitive deficits were found on measures of prefrontal functioning (e.g., WCST and Halstead Category Test). Both patient populations showed deficits using feedback to cue themselves to the correct response. Pulsifer (1996) provided similar support for the role of the cerebellum in the cognitive deficits, including inattentin, observed in a variety of developmental disabilities. In her review of five developmental disabilities associated with mental retardation (e.g., Fetal Alcohol Syndrome, Down's Syndrome, Fragile X Syndrome, Prader-Willi Syndrome, and Angelman Syndrome), she concluded that the neuroanatomical abnormalities common to all of these disorders were centered in the hippocampus and cerebellum. Furthermore, she concluded that the cognitive deficits common to all of the disorders were short-term memory problems, inattention, and deficient sequential information processing. While as Daum & Ackermann (1995) point out, conclusions about the specific involvement of the cerebellum in higher cortical functions are tentative because of the frequency with which patients with extracerebellar damage are included in research protocols, the literature does suggest that the cerebellum plays some role in the preparation for and appropriateness of cognitive processes.

Eye Movements

Reports on the neuropsychological functioning of patients with cerebellar damage include listings of associated neurological problems and often mention smooth pursuit dysfunction as an associated deficit (Akshomoff et al., 1992; Bracke-Tolkmitt et al., 1989). Problems with smooth pursuit, including anticipatory saccades as well as initiation deficits, have also been reported in studies specifically evaluating eye movement deficits in patients with cerebellar lesions or cerebellar degeneration. Several studies of patients with abnormalities localized to the cerebellum, resulting from cerebellar infarction or cerebellar degeneration, indicate that the region of the cerebellum that controls smooth pursuit eye movements is the posterior (dorsal) vermis or the underlying fastigial nucleus (Moschner, Zangmeister, & Demer, 1996; Vahedi, Rivaud, Amarenco, & Pierrot-Deseilligny, 1995). These patients with midline cerebellar abnormalities showed specific problems such as decreased rate of anticipatory smooth eye movements and decreased rate of smooth pursuit gain compared to controls. Additionally, smooth pursuit problems have also been found in patients with more widespread cerebellar damage, including neocerebellar and midline regions (Fetter et al., 1995; Pierrot, Amarenco, Roullet, & Marleau, 1990; Straube, Scheuerer, & Eggert, 1997). Fetter et al. found patients with idiopathic cerebellar damage, either restricted to or extending beyond the cerebellum, to show disturbed smooth pursuit when compared to control subjects. Similarly, Straube et al. (1997) found smooth pursuit deficits in each of ten cerebellar lesion patients. Specifically, these patients showed smooth pursuit initiation deficits toward the lesioned side. Half of these patients had lesions extending into the midline region of the cerebellum, while the remaining half had lesions in the

lateral hemispheres. Of the seven patients undergoing surgical removal of their astrocytoma, hemorrhage, or mestastisis of a carcinoma, two were evaluated before surgery, four were evaluated within one week of surgery, and one was evaluated within three weeks of surgery. Therefore, the results do not appear due to surgical or post-surgical interventions.

Further support for the hypothesis that smooth pursuit eye movements are controlled by the cerebellum comes from animal research. Straube et al. (1997) summarized research findings from activation studies in monkeys that indicated the ventral posterior interpositus nuclei is involved in smooth pursuit. Other studies using electrical stimulation paradigms with monkeys found that not only was the interpositus nuclei involved in the control of smooth pursuit eye movements, but also the dentate nuclei in the neocerebellar region was involved. Though the specific region within the cerebellum responsible for the control of smooth pursuit eye movements has not been clearly identified, a diverse body of research appears to support a role for the cerebellum.

Attention

As indicated previously, Heilman et al. (1997) referred to intention as a triage process that allows action to be prepared for. Intention has been further defined as comprised of four components: initiating an action, sustaining an action, inhibiting interfering actions, and shifting from one action to another (Denckla, 1996). It has been hypothesized that ADHD is a disorder of the third component of intention, namely behavioral inhibition (Barkley, 1997; Denckla, 1996). According to this model, children with ADHD appear inattentive not because they have a problem with attentional systems, but rather because they fail to inhibit ongoing behaviors or delay responding, both

processes necessary to execute a goal directed response. In this model, a failure to sustain attention arises from poor inhibition mechanisms that result in an inability to resist distraction. Impaired sustained attention abilities ultimately result from poor interference control, one aspect of behavioral inhibition. In other words, because of deficient interference control, either internal or external events disrupt the executive functions necessary to maintain on-task persistence. Similarly, a failure to shift attention appropriately results from failure to interrupt an ongoing response, another aspect of behavioral inhibition. According to this model, deficient behavioral inhibition in children with ADHD is thought of as the primary symptom, while impairments in subdivisions of attention, such as failure to encode, focus-execute, sustain, or shift, (Mirsky, 1989) are referred to as secondary symptoms.

The following section reviews the neuroanatomical substrates hypothesized to account for the secondary symptoms of deficient sustained and shifting attention and provides a link between the research on the cognitive functions of children with ADHD and the higher cognitive skills associated with the cerebellum.

Sustained Attention

According to the behavioral inhibition model of executive functions, deficient sustained attention, defined as an inability to maintain attention to a series of stimuli, results from poor interference control. According to this model, measures of selective attention, which specify the additional requirement of ignoring unspecified stimuli, can also be thought of as measures of sustained attention with the need for interference control heightened in the task. Based on a review of studies conducted on patients with injuries to the prefrontal cortex, Barkley (1997) noted that the right prefrontal cortex is

involved in tasks requiring inhibitory behavior that must be sustained over extended periods of time. In another study of 21 patients with frontal lobe lesions (divided according to predominant side of the lesion: left = 11, right = 10) and 16 controls matched for age, education, and handedness, patients with right frontal lobes lesions were found to have increased errors of omission on both the sustained and selective attention components of a visual CPT (Reuckert & Grafman, 1996)

Results from activation studies on healthy controls are consistent with the results reported on patients with frontal lobe lesions. Using an auditory discrimination paradigm during PET scanning, Cohen et al. (1988) evaluated regional brain metabolism in 27 healthy control subjects. Results indicated that while performing the auditory discrimination task, subjects had significantly higher glucose metabolic rates in the right middle prefrontal cortex compared with subjects at rest or receiving somatosensory stimulation. While this study is limited by a failure to use subjects as their own controls, the results lend support to the hypothesis that the right prefrontal cortex plays a role in auditory sustained attention. In a follow up study which also employed PET to study the regional brain activation in 27 healthy controls during completion of visual and a somatosensory sustained attention tasks, results also indicated activation in the right prefrontal cortex, as well as the right superior parietal cortex (Pardo, Fox, & Raichle, 1991). Activation in the right prefrontal cortex during the somatosensory discrimination task was observed during stimulation to both the right and left side of the body. The opposite pattern of activation was not observed. These results which were obtained on subjects used as their own controls, taken together with the results of the previous study,

suggest that the right prefrontal cortex is involved in the execution of sustained attention tasks across a variety of modalities.

In order to further elucidate the sites of increased regional cerebral blood flow during sustained attention tasks, Coull, Frith, Frackowiak, and Grasby (1996) used PET scans on eight healthy volunteers while they performed a rapid visual information processing task. Coull et al. (1996) found bilateral frontal and parietal activation when subjects executed this task. They suggested that the bilateral activation may have resulted from the addition of a working memory component to the more commonly employed test of simple sustained attention.

As indicated, research findings indicate significant elevations in glucose metabolism in frontal lobe regions in healthy controls during sustained attention tasks. Similar results have been obtained when evaluating adolescents diagnosed with ADHD (Zametkin et al., 1993). In a study comparing 10 adolescents diagnosed with ADHD (by structured interview) to 10 normal controls on a measure of auditory attention, results indicated that there were no statistically significant differences on measures of global cerebral glucose metabolism. Alternatively, glucose metabolism was significantly reduced in left frontal and basal ganglia regions and right temporal regions in adolescents with ADHD compared to the control subjects. While Zametkin et al. (1993) did not correct for multiple t-test comparisons, the results implicating the frontal lobes in sustained attention do not appear due to chance as three out of six of the significant reductions were found in the left frontal region. Furthermore, decreased metabolism in the left anterior frontal region was significantly correlated with increased severity on six behavioral measures including teacher's ratings of conduct problems, hyperactivity, and

inattentiveness on the Conners' Teachers Rating Scale. Ultimately, research findings indicate that while laterality remains uncertain, the frontal lobe regions clearly plays a role in sustained/selective attention abilities.

Shifting Attention

While evidence clearly points to involvement of the right prefrontal cortex in the execution of sustained attention tasks, a primary neuroanatomical substrate associated with shifting attention has not been as clearly delineated. Three areas that have been implicated include the cerebellum, basal ganglia, and frontal cortex.

A series of studies completed with patients with cerebellar lesions lends evidence to the hypothesis that the neocerebellum contributes to the ability to shift cognitive set (Akshoomoff & Courchesne, 1992, 1994; Courchesne et al., 1994). In their original study, Akshoomoff and Courchesne (1992) evaluated five children (mean age at testing = 8.6 years) who had undergone surgical resection of cerebellar astrocytomas and one adult patient with idiopathic cerebellar degenerative disorder. MRI or CT scans showed that two children had lesions to the lateral cerebellar hemispheres (one right and one left) as well as the corresponding ventrolateral dentate nucleus, one child had damage to the left lateral cerebellar hemisphere only, one child evidenced damage to the superior cerebellar peduncle, and the remaining child showed a small focal unilateral lesion outside of the neocerebellar region. The adult patient was described as having extensive parenchymal volume loss. Each of the subjects completed two tasks. The first task tested ability to sustain attention to infrequently presented visual stimuli while ignoring all other stimuli (i.e., frequent visual stimuli, frequent auditory stimuli, and infrequent auditory stimuli). The second task assessed ability to respond to the first infrequent stimuli from one

modality, then shift attention to respond to the first target stimuli from the second modality, than shift back to the first modality, and so on. Results indicated that patients with cerebellar damage performed similar to age and IQ matched controls on the sustained attention task, but the patients were significantly impaired in their ability to rapidly shift their attention. In other words, when a target in the new modality occurred less than 2.5 seconds after a cue to shift attention (i.e., a target from the previous modality), the "hit" rate for the patients with cerebellar lesions was significantly less than the "hit" rate for the controls. (Hit rate was defined as the percentage of correctly detected targets.) The researchers concluded that the patients' inability to shift attention could not be accounted for by motor control problems because they were not impaired on the sustained attention task with the same motor requirements. Furthermore, results do not appear to be influenced by post-surgical treatment effects as only two children received focal irradiation and none received chemotherapy. The patients with cerebellar damage did not appear to have difficulty disengaging attention as they correctly ignored stimuli in the same modality after a cue to shift attention. However, when only a short period of time lapsed between the cue to shift and the target stimuli in the new modality, the patients frequently failed to reingage. Akshoomoff and Courchesne (1992) concluded that a failure to rapidly shift attention may depend on lesion location because the patient whose lesion spared the neocerebellar region did not show any evidence of a shifting attention deficit. The strength of the conclusion localizing control of shifting attention abilities within a specific area of the cerebellum is limited by the fact that only one patient with non-neocerebellar lesions was evaluated. Furthermore, they provided evidence of normal shifting attention abilities in non-cerebellar lesion patients (i.e medial

temporal lobe, right occipital pole-parietal lobe, and right mesial frontal pole lesions) as further support for the localization of this ability to the cerebellum.

In a follow-up experiment, Courchesne et al. (1994) evaluated the same sustained attention and intermodality shifting attention abilities in children with autism. They found that these children (N = 8) were not significantly impaired on the focus attention portion of the task. However, the autistic children were significantly worse than either chronological age matched or mental age matched controls at detecting hits when 2.5 seconds or less had elapsed since the presentation of the last target. Secondary to findings that seven of the eight autistic children had significant vermal hypoplasia (and the eighth child had significant vermal hyperplasia), Courchesne et al. (1994) argued that the shifting attention deficits in autistic children further supports the hypothesis that the cerebellum plays an important in attention. Contrary to the results of the previous study, the cerebellar abnormalities were not localized to the neocerebellum, yet shifting attention deficits were still found.

In the third study in their series assessing shifting attention abilities, Akshoomoff and Courchesne (1994) re-evaluated the same patients, this time using a within modality shifting attention paradigm. Again, the first part of the experiment required subjects to maintain a focus of attention and respond to infrequently presented stimuli within one category. However, in the shifting attention portion of this experiment, the patients were required to shift between two different categories of stimuli within the visual domain (i.e., respond to a target shape stimuli and than a target color stimuli). Again, results indicated that the patients with neocerebellar damage had significantly poorer performance versus the control children on the shift attention task. It is also noteworthy

that the patients with cerebellar damage performed slightly worse on a measure of false alarm rates in the intramodality shifting attention experiment versus the intermodality shifting attention paradigm while the normal controls showed approximately the same error rates across tasks.

The results from the Akshoomoff and Courchesne series implicating the cerebellum in shifting attention ability were further supported by a functional imaging study conducted on healthy adult subjects (Le, Pardo, Hu, 1998). During this experiment, subjects completed four different tasks while undergoing fMRI. The four tasks were visual fixation, sustained attention to color, sustained attention to shape, and shifting attention within modality. The shifting attention task was similar to the paradigm employed by Akshoomoff and Courchesne (1994). Accuracy rates were greater than 80% and not significantly different between the sustained and shifting attention tasks. Contrasts between each of the tasks were conducted in order to highlight the activation within specific cerebellar regions associated with the increased task demand. The contrast between sustained attention and visual fixation (which highlights the added motor component of the sustained attention task) showed significant activation in the anterior lobe of the cerebellum ipsilateral to hand used to make the key presses. Results indicated that the contrast between the shifting and sustained attention tasks most consistently activated an area of the right lateral cerebellum. Residual activation in the folium and posterior parietal regions was also found. These findings suggest that the shifting component of the task is associated with activation to the neocerebellum and possibly parietal lobe. These results were replicated in a second study conducted on the second half of the sample using an alternate fMRI measurement technique, however, in

this study, bilateral activation of the lateral cerebellum and the posterior superior parietal lobule was found.

Although the previous studies suggest that the cerebellum plays a role in ability to shift attention, evidence also exists to support an hypothesis that shifting attention abilities are maintained by frontal-subcortical structures. For example, many studies have reported that patients with Parkinson's disease (who evidence basal ganglia dysfunction) are impaired on tasks requiring cognitive shifts of attention (Hayes, Davidson, Keele, & Rafal, 1998; Owen, et al, 1993; Tamaru, 1997). Owen and colleagues also found patients with either right or left frontal lobe lesions to be deficient on their task designed to measure set shifting. Furthermore, although the WCST assesses problem solving and planning abilities in addition to shifting attention abilities, fMRI studies which show activation in the frontal lobe region during execution of this task suggest that frontal lobe regions may be also be linked with shifting attention abilities (Volz et al., 1997).

Research on a three groups of neurosurgery patients, also found deficits in the frontal lobe group on a task requiring an extra-dimensional shift of attention (Owen, Roberts, Polkey, Sahakian, & Robbins, 1991). These groups included 20 patients with frontal lobe excisions (secondary to aneurysms, meningiomas, benign tumors, or arterio-venous malformations), 20 intractable epilepsy patients with medial and temporal pole resection, and 11 intractable epilepsy patients with amygdalo-hippocampus removal. An extra-dimensional shift was defined as one that required the subject to shift response set to a previously irrelevant dimension (versus an intra-dimensional shift that required a shift to a novel target in the same stimulus dimension). The set shifting paradigm was

reported to assess a similar process as the core shifting component of the WCST without the confounds of additional cognitive requirements (i.e., problem solving). The impaired frontal lobe lesion group included ten patients with right and one left frontal pole excisions, two right lateral surface excisions, one right and one left medial surface excision, one right and two left unilateral lobectomies, and two bilateral lobectomies. Analyses indicated that failure on the shifting attention task could not be more specifically related to lesion location within the frontal lobes.

Information about the ability of children with ADHD to shift attention either across or within modality is limited. As indicated in the review of executive functioning in children with ADHD, the WCST may be thought of as a measure of ability to shift attention within modality in response to examiner feedback. Studies that have included the WCST as part of a neuropsychological test battery employed to differentiate between children/adolescents with ADHD and normal controls found significant results for variables such as failure to maintain set, trials to first category, and perseverative responses. Though these results suggest that children with ADHD have difficulty shifting attention, as indicated, it has also been suggested that the WCST should be thought of primarily as a measure of problem solving/hypothesis testing ability (Barkley, 1994). Furthermore, two of the three variables found to differentiate children with ADHD from normal controls on the WCST pertain to measures of disinhibition/failure to sustain attention (e.g., failure to maintain set or trials to first category) rather than a failure to shift attention.

Other studies report use of cued reaction-time tests in order to assess shifts of attention in children with ADHD (Swanson et al., 1991). The results indicate that

children with ADHD have significant deficits in reaction time, however the conclusions that can be drawn from these tasks are limited by the requirement that the subjects show an ability to use a cue to shift their visual attention across the visual field space rather than an ability to shift cognitive set. The researchers interpreted these results as representative of a failure to sustain focused attention to the cue rather than an indication of failure to shift attention to the target. The primary difference between cued reaction-time tasks and tasks requiring a cognitive shift of attention is that the later uses stimuli with multiple dimensions which the subject must shift his/her attention between (e.g., color and shape) according to instruction specifications. Alternatively, the former uses stimuli with only one dimension (e.g., location) that must be attended to and therefore does not require this internal shift of attention between dimensions. Therefore, while preliminary research suggests that children with ADHD may be impaired in their ability to shift attention, conclusions remain tentative because of the use of measures lacking primary construct validity for an ability to shift cognitive set.

Summary and Rationale

Ample evidence currently exists to indicate that children diagnosed with ADHD show deficits on measures of sustained attention. However, research is limited with regard to the ability of children with ADHD to perform cognitive shifts of attention. The present study was designed to examine sustained and shifting attention abilities in children with ADHD compared to a normal control group. A computerized measure of shifting attention that specifically assesses ability to shift cognitive set within a single sensory modality was employed.

The literature reviewed regarding the neuroanatomical substrates involved in the execution of sustained attention tasks clearly supports a role for the frontal lobes. Research on the neuroanatomical substrates thought to be involved in the execution of cognitive shifts of attention suggests that the cerebellum likely plays a role. However, research in this area remains inconclusive because of conflicting evidence from studies showing that frontal lobe regions or basal ganglia structures may also be involved in an ability to shift attention.

Similar to the conflicting research findings pertaining to the neuroanatomical substrates associated with shifting attention deficits, research that has attempted, using neuroimaging techniques, to localize the neuroanatomical dysfunction associated with ADHD has found abnormalities within the cerebellum, basal ganglia, and/or frontal lobe region. Therefore, a secondary purpose of this investigation is to provide support for the idea proposed by Denckla (1998) and others (e.g., Voeller & Heilman, 1988) that ADHD likely involves dysfunction in multiple regions including cerebellar and prefrontal regions.

The literature reviewed clearly indicates that children with ADHD show deficits on measure of sustained attention as well as other executive functions found to be sensitive to the effects of frontal lobe lesions. As indicated, one such measure that appears to be sensitive to detecting ADHD and deficient frontal lobe functioning is the Stroop test. More specifically, impaired scores on the interference portion of the Stroop test were associated with right lateral prefrontal cortex lesions (Vendrell et al., 1995). Furthermore, research using PET scanning techniques with healthy control subjects found activation in the right orbital frontal region during performance of the interference

portion of the Stroop test (Bench et al., 1993). Activation in the prefrontal regions of the right cortex was attenuated by task alterations that maximized the differential requirements for sustained attention across a series of tasks conducted during the functional imaging session. Therefore, because of its reportedly high sensitivity, the Stroop test was used as a measure of frontal lobe region dysfunction.

While performance on a variety of neuropsychological tests appears to be indicative of frontal lobe functioning, there are no neuropsychological measures available to assess cerebellar functioning. Alternatively, neurological examinations have been specifically designed to assess for cerebellar dysfunction. Specifically, the literature strongly indicates that the cerebellum controls smooth pursuit eye movements. Therefore, assessment of smooth pursuit eye movements was used to evaluate cerebellar dysfunction. While it was expected that children with ADHD would show a significantly greater frequency of saccades off target, it was not expected that this problem will be a function of a more basic difficulty fixating on an image. Support for this notion comes from research of Kemner, Verbaten, Cuperus, Camfferman, and van England (1998) who compared children with autism or ADHD to normal controls on their ability to maintain focus to frequently presented stimuli. Results indicated that only the autistic children had significantly more saccades during visual fixation compared to the other two groups.

In order to support the hypothesis that deficits in ADHD are due to dysfunction in multiple neuroanatomical regions, results from the sustained attention task in children with ADHD were correlated with a measure shown to be sensitive to frontal lobe dysfunction (i.e., the Stroop test), and results from the shifting attention task in children with ADHD were correlated with results from a measures known to be sensitive to

cerebellar functioning (i.e., smooth pursuit eye movements). Evidence of dysfunction on both frontal and cerebellar tasks in children with ADHD would be suggestive of involvement of the frontal-subcortical-cerebellar system in the dysfunction associated with the disorder. These findings would be consistent with the developmental chronometry hypothesis which suggests that these regions and their interconnections are particularly vulnerable because of their protracted course of development.

Ultimately, according to this framework, ADHD may be thought of as a dysfunction of the intentional system whereby children show problems with initiating an action (behavioral or cognitive), sustaining an action, inhibiting off-task actions, and shifting from one action to another secondary to neuroanatomical dysfunction involving the frontal-subcortical-cerebellar system.

Greater understanding of the behavioral dysfunction associated with ADHD will hopefully result in improved understanding of the neuroanatomical dysfunction and eventually etiology and most effective treatments for the disorder.

Hypotheses

1. Children diagnosed with ADHD will score significantly worse than healthy control children on a sustained attention task.
2. Children diagnosed with ADHD will score significantly worse than healthy control children on a shifting attention task.
3. Children diagnosed with ADHD will score significantly lower than controls on the interference portion of the Stroop test.
4. Children diagnosed with ADHD will exhibit a significantly greater frequency of saccades versus controls during a smooth pursuit task

5. Performance on the shifting attention task will be negatively correlated with the frequency of saccades made during the smooth pursuit task.
6. The Stroop test interference score will be positively correlated with performance on the sustained attention task.

CHAPTER 2
METHODS

Participants

Participants included 31 children diagnosed with ADHD and 31 normal controls. Only children between the ages of 8 and 12 years were asked to participate. The lower limit of 8 years was used for two primary reasons. First, Akshomoff and Courchesne (1994) found that normal control children with a mean age of 9.6 years (SD = 1.5 years) were able to correctly shift attention with a high percentage of accuracy (hit rate > 85%) on a computerized task similar to the one developed for this study (described in detail below). Therefore, keeping the age range of the children in this study to within one standard deviation of the mean in the Akshomoff and Courchesne (1994) study helped to ensure that any impaired ability to complete the task was not due to the age of the child. Second, research findings suggest that a spurt in development of executive functions (including planning, verbal mediation, working memory, and selective action) occurs between the ages of 5 and 7 years (Welsch, Pennington, & Groisser, 1989). Therefore, rapid advances in executive function abilities appear before children reach 8 years old. All participants in the study spoke English as their first language. Children were not excluded from either group according to sex, race, ethnicity, or handedness.

Children were included in the ADHD group if they met 2 of 3 of the following criteria: (1) previously diagnosed with ADHD by a child psychologist, neuropsychologist, pediatric neurologist, or developmental pediatrician, (2) met DSM-IV

diagnostic criteria for ADHD at the time of the study, and/or (3) received a t-score > 68 on the ADHD Index of the Conners' Parent Rating Scale – Revised (Conners, 1997b). According the Conners' Rating Scale – Revised User's Manual, the ADHD Index is the most appropriate scale on the measure for identifying children who are at risk for obtaining an ADHD diagnosis. Additionally, normative data indicate that children diagnosed with ADHD according to DSM-IV criteria score significantly higher than a nonclinical control group as well as an emotional problem control group on the ADHD Index (Conners, 1997a). T-scores > 70 (> 98th percentile) are defined as markedly atypical and indicative of significant problems. Furthermore, using a cut-off above the 98th percentile reduces the likelihood of false positive diagnoses (Barkley, 1998). Due to difficulty with subject recruitment, a t-score > 68 on the ADHD Index (which equals a t-score > 70 minus 1 SEM) was adopted as the cut-off criteria.

Children with a Full Scale IQ (FSIQ) < 82 (85 - 1 SEM) were excluded from the study. This score was chosen as a cut-off based on results of the Akshomoff and Courchesne (1994) study. The mean Full Scale IQ (FSIQ) of their normal controls was in the Average to High Average range (mean =110.1, SD = 7.6). We therefore set out to recruit children with at least average FSIQ's. While it is not known whether children with below average FSIQ scores would have been able to complete the task, they were excluded from participation in this study in order to help ensure that dysfunction on the shifting attention task was due to attentional/intentional dysfunction rather than an inability to understand the task.

Children were excluded from both groups if they had evidence of a learning disability based on a brief screening. Specifically, learning disability was defined as a

WRAT3 Spelling subtest score < 7th percentile (standard score < 78, Z = -1.5; see Korkman & Pesonen, 1994). Children were also excluded from both groups if there was evidence of a major sensory or motor handicap (e.g. paralysis, deafness, blindness), if they were reported to have a comorbid neurological condition, or if they met criteria for an Axis I diagnosis. However, because of the high comorbidity between ADHD and Oppositional Defiant Disorder (ODD), children in the ADHD group who also met DSM-IV screening criteria for ODD were not excluded.

Measures

Demographic Information

All primary caregivers completed a short demographic questionnaire (see Appendix A). The questionnaire provided basic demographic data such as age, sex, and race/ethnicity of the child. Information was also collected on the medical/psychological diagnostic history, current medications, and educational history of the child. Finally, the questionnaire included demographic information on the primary caregiver, including highest grade completed, occupation, income, and family history of ADHD, LD, or other psychiatric history.

Disruptive Behavior Disorders Evaluation

Conners' Parent Rating Scale – Revised (CPRS). The CPRS is a parent report rating scale used to evaluate evidence of psychopathology and disruptive behaviors in children and adolescents by providing information on the presence of both internalizing and externalizing symptoms in the last month (Conners, 1997b). The CPRS consists of 80 items rated on a scale of 0 (Not at all true) to 3 (Very much true). The most recent

revision of the CPRS specifically assesses for DSM-IV diagnostic criteria of ADHD. The CPRS contains 14 subscales including Oppositional, Cognitive Problems, Hyperactivity, Anxious-Shy, Perfectionism, Social Problems, Psychosomatic, Conners' Global Index, Conners' Restless-Impulsive Index, Conners' Emotional Lability Index, ADHD Index, DSM-IV Symptoms subscale, DSM-IV Inattentive subscale, DSM-IV Hyperactive-Impulsive subscale. Raw scores are converted to T-scores separately for males and females and across five age groups (3-5, 6-8, 9-11, 12-14, and 15-17).

The CPRS was normed on over 2,400 boys and girls between the ages of 3 and 17. Six to eight week test-retest reliability coefficients range from .60 to .90. Construct validity for the CPRS is available from factor analysis studies. The first five subscales listed above were factor derived. Low to moderate correlations (mean = 0.33) were found among these subscales, suggesting that they assess distinct problems. Criterion validity for the CPRS was established by comparing the scores of adolescents in three groups: nonclinical, ADHD, and emotional problems. Results indicated that the ADHD group scored significantly higher than the nonclinical group on all subscales except perfectionism. Further, the scores for the ADHD group were significantly different from the emotional problems group on all subscales except Anxious-Shy, Psychosomatic, and Conners' Global Emotional Lability Index. Convergent validity for the CPRS has also been established. Specifically, the CPRS Cognitive Problems subscale and the DSM-IV Inattentive subscale were positively correlated with an Overall Index Score on the Conners' CPT (Conners, 1997a).

As indicated, the ADHD Index was the primary subscale of interest from the CPRS because of its ability to distinguish among children with ADHD, emotional problems, and nonclinical controls.

DSM-IV Structured Interview for Disruptive Behavior Disorders. All primary caregivers also completed this structured interview which reviews diagnostic criteria for Conduct Disorder, Oppositional Defiant Disorder, and Attention-Deficit/Hyperactivity Disorder. Diagnostic criteria for Separation Anxiety Disorder and Major Depressive Episode were also included. The caregiver was asked to rate their child on a scale from 1 (i.e. rarely) to 4 (i.e. very often) on how often he/she displays each of the listed symptoms. Ratings of 3 or 4 are considered indicative of significant symptom. The list of endorsed symptoms were then compared to DSM-IV diagnostic criteria.

Intelligence Measure

Wechsler Intelligence Scale for Children-Third Edition (WISC-III). The WISC-III is the most recent edition of a measure of general cognitive functioning for children between the ages of 6 years and 16 years, 11 months (Wechsler, 1991). Three IQ scores [Full Scale IQ (FSIQ), Verbal IQ (VIQ), and Performance IQ (PIQ)] and four Index scores (Verbal Comprehension, Perceptual Organization, Freedom from Distractibility, and Processing Speed) with a mean of 100 (SD = 15) are obtained. The Verbal subtests include Information, Similarities, Arithmetic, Vocabulary, Comprehension, and Digit Span. The Performance subtests include Picture Completion, Coding, Picture Arrangement, Block Design, Object Assembly, and Symbol Search.

The WISC-III was normed on a sample of 2,200 children who were stratified according to age, gender, race/ethnicity, geographic region, and parent education

consistent with the 1988 U.S. census. Split-half reliability ranged from .69 to .87 on the individual subtests, .85 to .94 on the Index scores, and .91 to .96 on the IQ scores. According to a study of a subgroup of the standardization sample, WISC-III scores have adequate test-retest reliability with Performance subtests showing slightly higher practice effects than the Verbal subtests. Average stability coefficients across all ages ranged from .64 to .89 on the subtests, .82 to .93 on the Index scores, and .87 to .94 on the IQ scores. Convergent validity of the WISC-III is provided by intercorrelation coefficients of the subtests which indicate that Verbal subtests correlate more highly with other Verbal subtest than with Performance subtests and vice versa. Factor analytic techniques which resulted in a four factor solution (i.e. Index scores) provide further evidence of internal validity of the WISC-III. Moderate correlations between WISC-III IQ scores and school grade point averages (ranging from .28 to .48) or achievement test scores (ranging from .11 to .74) provide further evidence of convergent validity.

Achievement Measure

Wide Range Achievement Test – 3rd edition (WRAT3). The WRAT3 is a measure of achievement that is divided into three subtests: Reading, Spelling, and Arithmetic (Wilkinson, 1993). Re-standardization of the WRAT was conducted on a nationally stratified sample of people chosen to represent the 1990 U.S. census on the characteristics of gender, ethnicity, regional residence, and socioeconomic status. Convergent validity for the WRAT3 was determined through correlations with the California Test of Basic Skills, the California Achievement Test, and the Stanford Achievement Test. Correlations ranging from .41 to .87 suggest that the WRAT3 is a valid measure of achievement. Criterion validity for the WRAT3 has been established by

showing that test scores can distinguish among groups of gifted, learning disabled, mentally retarded, and normal students. Reliability coefficients were calculated on the WRAT3 by using coefficient alpha, by comparing alternate forms, and by calculating test-retest stability coefficients. The reliability coefficients for the various WRAT3 subtests ranged from .80 - .98. Across procedures employed, reliability coefficients for the spelling subtest fell at or above the reliability coefficients for the reading and arithmetic subtests, suggesting that this subtest is stable across time.

Raw scores on the WRAT3 are converted into standard scores with a mean of 100 and a standard deviation of 15. Standard score tables are available for 32 age groups. In addition to standard scores, grade scores and percentile equivalents are available.

Attention Measures

Stroop Color and Word Test (Stroop). The Stroop is a speeded test measuring ability to inhibit responding to salient information (Golden, 1978). The Stroop is divided into three sections and provides three scores: word score, color score, and color-word score. In each section, the subject is required to respond, as quickly as possible, to the stimuli found in five columns (with 20 items in each column). In the first section, the subject is required to read a randomized list of words consisting of the names of three colors printed in black ink. The second condition requires the subject to state the color of the ink used to print randomized lists of four X's (i.e., XXXX). The final condition, referred to as the interference condition, requires the subject to state the color of the ink used to print conflicting color names. The third condition is reported to be sensitive to a failure to inhibit a more salient response (Golden, 1978). Normative data, which convert

raw scores to T-scores (mean = 50, SD = 10) are available for children between 7 – 16 years.

Test-retest scores on the Stroop tests (covering periods ranging from 1 minute to 10 days) indicate adequate reliability, ranging from .69 to .89 across various versions of the test. Validity of the Stroop as a screener of brain dysfunction has been established through studies of patients with unilateral brain lesions. More specifically, a pattern of normal scores on the first two conditions of the task (word score and color score) with low color-word (interference) scores was associated with isolated prefrontal brain lesions (Goldman, 1979).

In addition to the three scores provided by the different conditions, a pure interference score can also be calculated. The interference score, which is derived by subtracting a predicited color-word score from the raw color-word score, is thought to be a purer measure of cognitive inhibition because it accounts for the subjects' processing speed (Boone, Pontón, Gorsuch, González, & Miller, 1998). Higher scores indicate that the subject has greater cognitive flexibility and is less susceptible to interference (Goldman, 1979). Because the interference score accounts for the subject's processing speed, this score was used in the final analyses.

Computerized sustained and shifting attention tasks. The computerized sustained and shifting attention tasks were presented on a Dell Inspiron 3200 personal laptop computer. Visual stimuli were displayed on a 16 bit, high resolution 14 inch color screen. For both the sustained and shifting attention tasks, the stimuli consisted of black outline drawings of a circle and a triangle and solid orange and blue squares. All stimuli were randomly ordered and each stimulus was displayed in the center of the screen for a

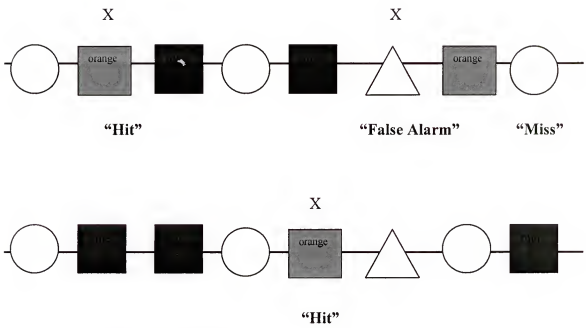
duration of 100 ms. The interstimulus intervals varied randomly between 600 ms and 1500 ms (at ten equal intervals). The stimuli subtended approximately 1.4 of the central visual field (adapted from Akshoomoff & Courchesne, 1994; Le, et al., 1998). SuperLab Pro Experimental Lab Software was used to design the experiments, run them on subjects, and collect the data for both the sustained and shifting attention paradigms.

Each subject completed three types of tasks: sustained attention to color, sustained attention to shape, and shifting attention between visual categories (color and shape).

Sustained attention tasks. The sustained attention tasks were designed to assess ability to maintain attention and respond to infrequently presented stimuli in one category (i.e., the color orange) while ignoring the frequently presented stimuli in that category (i.e., the color blue) as well as both the frequent and infrequent stimuli in the second category (i.e., circular and triangular shapes). The design of this sustained attention task is similar to many of the CPT's referred to in the literature review (i.e., includes rapid presentation of a long series of stimuli, requires subjects to respond to a designated target, and presents the target at a low probability rate with a constant externally paced rate). Both split-half and test retest reliabilities for the CPT have been shown to be high, equaling 0.88 (Cornblat & Keilp, 1994). While prior research on CPT's suggests that these types of tasks may be sensitive to discriminating children with ADHD from normal controls, results indicating that numerous populations perform poorly on the task also suggest that deficits are not likely to be specific to children with ADHD.

Sustained attention to color. Subjects were instructed to maintain visual focus on the center of the screen. They were further instructed to respond by pressing the space

bar whenever the rare target color, orange, appeared (p = 0.25). Subjects were told to ignore any shape information (i.e., frequent circles and rare triangles) and to respond as quickly as possible to the designated color stimulus. All subjects completed a block of practice trials with the investigator before beginning the actual task. As shown in Figure 2, each correctly detected rare orange target was scored as a "hit", while each incorrectly detected rare triangle was scored as a "false alarm". Any failure to respond to a rare orange target was labeled a "miss". False alarms are essentially the equivalent of commission errors commonly referred to in CPT literature, while misses are the equivalent of omission errors. "False presses" (i.e., responses to frequently presented circles or blue targets) were also calculated.



Note. X = subject's key press response

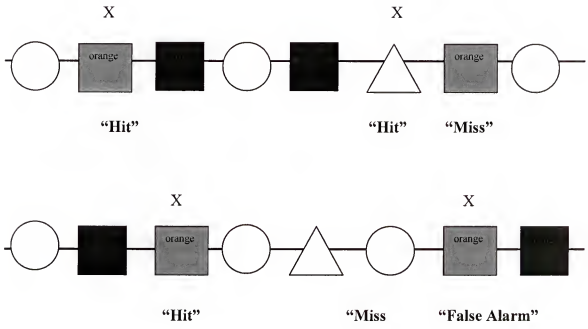
Figure 2.
Schematic Drawing of Computerized Sustained Attention to Color Task:
(Target = Orange)

Sustained attention to shape. Subjects were instructed to maintain visual fixation on the center of the screen. They were further instructed to respond by pressing space bar whenever the rare target shape, a triangle, appeared ($p = 0.25$). Subjects were told to ignore any color information (i.e., frequent blue targets and rare orange targets) and to respond as quickly as possible to the designated form stimulus. All subjects completed a block of practice trials with the investigator before beginning the actual task. Each correctly detected rare triangle was scored as a "hit", while each incorrectly detected rare orange target was scored as a "false alarm". Any failure to respond to a rare triangle was labeled a "miss". "False presses" (i.e., responses to frequently presented circles or blue targets) were also calculated.

Shifting attention task. The shifting attention task was designed to assess ability to respond to infrequently presented stimuli in one category (e.g., color = orange) than disengage attention from that category and shift attention to the rare stimulus in the second category (e.g., shape = triangle). While normative data is not available on this type of shifting attention task, the only requirement above and beyond that of the sustained attention task is a requirement to switch attention between visual targets. Therefore, the face validity of the task is high. Furthermore, as a review of the literature indicated, the shifting attention task is useful at differentiating groups of subjects with neurological impairment (e.g., patients with cerebellar lesions or autism from control subjects).

Subjects were instructed to maintain central fixation. They were further instructed to respond to the target stimulus by pressing the space bar. The target stimulus alternated between the rare orange target and the rare triangle. The subject was instructed

to respond to the first target stimulus in one category, then shift their attention to the other category and respond to the first target stimuli in that category, and so forth. Choice of target stimulus depended on shifting attention between appropriate color and shape information. All subjects completed a block of practice trials with the investigator before beginning the actual task. Figure 3 provides a schematic drawing of the requirements for the shifting attention task.



Note. X = subject's key press response

Figure 3.
Schematic Drawing of Computerized Shift Attention to Task:
(Targets = Orange and Triangle)

Eye Movement Measurements

As originally proposed, an Applied Science Laboratories (ASL, Waltham, MA) 4000 SU eye movement system was to be used to collect data on eye movements. The 4000 SU system is a video-based monocular corneal reflection system that measures the

point of gaze relative to a video image recorded by a headband-mounted scene camera. The system has the capability to measure pupil position and corneal reflex which are used to compute visual gaze with respect to the optics. Therefore, the root-mean-square error (RMSE) and the frequency of anticipatory saccades could be evaluated in the frame by frame analysis. RMSE (obtained by squaring the difference between eye position and target position for all intervals of pursuit tracking and then obtaining the average of the square root of these numbers) and frequency of saccades were chosen as the dependent measures of smooth pursuit eye movements based on the efficacy of these measurements shown in previous research. Though assessment of smooth pursuit has not been conducted on ADHD probands, research has shown that children with ADHD exhibited more premature saccades than normal control children on an oculomotor delayed response task (Ross et al., 1994). Furthermore, studies on populations suspected of having smooth pursuit deficits (e.g., schizophrenics) have shown the utility of saccadic frequency measurements. For example, frequency of saccades during smooth pursuit has been shown to correlate with symptom severity in a chronic schizophrenic group (Ciuffredo, Alpert, Blackstone, Fudge, & Thaler, 1994). Furthermore, test-retest reliability of measurements of saccadic frequency during pursuit has been assessed. Results suggest that this oculomotor function is stable across morning and afternoon assessments as well as across four weekly intervals (Roy-Byrne, Radant, Wingerson, & Cowley, 1995).

The importance of quantifying the degree of smooth pursuit impairment rather than indicating only presence or absence of smooth pursuit failure (i.e., presence or absence of anticipatory saccades) is highlighted by studies which show that the smooth

pursuit system does not fully develop until late adolescence (Katsanis, Iacono, & Harris, 1998; Ross, Radant & Hommer, 1993). These findings suggest that school age children without clinically significant impairments in their smooth pursuit system may nonetheless exhibit some deficits on smooth pursuit tracking and associated anticipatory saccades. Therefore, deficits on smooth pursuit tasks due to developmental changes must be differentiated from those that are indicative of underlying dysfunction.

Due to an inability to calibrate the video-based monocular corneal reflection system on children, electro-ocular gram (EOG) recordings were used to collect eye movement information while the child performed the smooth pursuit tracking task. With this format, electrodes were placed lateral to both the left and right eyes to record horizontal muscle movements. A grounding electrode was placed on the child's forehead. The child was seated 43.5 cm away from the computer screen (with accurate distance from the screen maintained by the use of a chin rest).

Each child was asked to keep his/her eyes on the target and follow it to the best of his/her ability. The target consisted of a bright square against a black background. During the smooth pursuit tracking task, the target moved horizontally back and forth over 30° with a constant velocity of 10°/second and a 1.4 second fixation between changes in direction (adapted from Ross et al., 1993). The target underwent four changes to the opposite direction. Each child completed the smooth pursuit task twice in order to ensure accurate recording of ocular movements and to ensure that each child understood the task. Only the second recording from each child was used in the analyses. The time to complete the entire smooth pursuit task was approximately 5 minutes.

AcqKnowledge software (BIOPAC systems, Inc., 1998) was used to interpret EOG recordings. For each subject, a sin wave form, with the positive slope of the sin wave representing eye movements to the right and the negative slope representing eye movements to the left, was displayed. To begin analysis of saccadic frequency, each subject's sin wave form was superimposed on the smoothed wave of his/her eye-movements. Next, the number of square wave deviations from the sin wave, that followed a period of matching, was calculated. Square wave deviations were defined as any obvious deviations away from the slope that were square in shape and recovered to the original sin wave. The squareness represents the eyes moving away form the target, temporarily maintaining position, and finally returning to the target. Saccades in the direction of the target that increased position error were classified as anticipatory saccades. Therefore, only square wave deviations in the same direction as the slope of the wave form were calculated, as these deviations represented excessive eye movements in the same direction as the smooth pursuit.

An attempt was made to use voltage-based measurements to define the minimal size of a square wave deviation necessary to be labeled a saccade. However, this procedure was unsuccessful as the voltage scale varied across subjects. In order to circumvent this problem, two independent raters calculated the total number of square wave forms during each subject's smooth pursuit task. Both raters were blind to group. Inter-rater reliability was calculated on all 43 children who completed the eye-movement task. Inter-rater reliability was calculated at .89.

Procedure

ADHD children were recruited through a tertiary care clinic at a university based hospital or through the private practice of a local neuropsychologist. All children being evaluated for ADHD between the ages of 8 years - 0 months and 11 years - 11 months were asked to participate, as were children returning for follow-up appointments who had already received a diagnosis of ADHD. Normal control children were recruited through advertisements posted in a hospital newsletter, the university newspaper, a local paper, or at an after-school activity center. The procedure for the study and University of Florida Institutional Review Board (IRB) consent forms were reviewed with all potential participants. Written consent (from primary caregivers) and verbal assent (from children) was obtained prior to any testing. All subjects were told that their participation was voluntary, and that they could withdraw their participation at any time. All subjects were paid $5 for their participation in each phase of the study.

The initial phase of the study involved screening potential children for exclusionary criteria. Primary caregivers completed the Conners Parent Rating Scale to screen for ADHD symptomatology. They also completed the DSM-IV Structured Interview for Disruptive Behavior Disorders to screen for comorbid diagnoses. Children completed the Block Design and Vocabulary subtests of the WISC-III. These subtest scores were used to prorate a FSIQ score according to the procedure for obtaining deviation quotients for Wechsler short forms outlined in Sattler (1992). Deviation quotients (which account for individual subtest reliability and intercorrelations) were calculated according to the following equation:

Deviation Quotient = (composite score x a) + b
where a = 15/S
b = 100 – n(150)/S
S = the standard deviation of the composite score
n = the number of component subtests

such that the equation for calculating a deviation quotient using the Vocabulary and Block Design subtests was [(composite score)(2.9) + 42]. Children also completed the Reading, Spelling, and Aritnmetic subtests of the WRAT3 as a screening for comorbid learning disabilities. Learning disability was defined as a score falling $\geq$ 1.5 standard deviations below the mean ($\leq 7^{th}$ percentile) on the Spelling subtest of the WRAT3 (Barkley, 1998; Korkman & Pesonen, 1994). Children went on to complete the final two phases of the study if they did not meet criteria for a comorbid Axis I diagnosis (other than ODD), if their prorated IQ was greater than 82, and if they did not show evidence of a learning disability.

The second phase of the study, conducted immediately following the screening phase, consisted of the Stroop and the computerized sustained and shifting attention tasks. Order of test administration across phases I and II was consistent across children, beginning with the WISC-III subtests, and followed by the WRAT3, Stroop, and computerized attention tasks.

For each of the computerized sustained attention tasks, after completion of a block of practice trials, each subject was presented with five trial blocks of 80 stimuli in each block (40 shape stimuli and 40 color stimuli). Selection of the category to be attended to first (i.e., color or shape) was counterbalanced across subjects. Following administration of the first sustained attention tasks, subjects were administered 10 trial blocks of the shifting attention task. Finally five trial blocks of the second sustained

attention task were administered. Total testing time for the sustained and shifting attention tasks was approximately 30 minutes. Hit, miss, false alarm, or correct rejection was tabulated for each stimuli.

All testing was completed in a quiet testing room either on the day of the child's medical/neuropsychological evaluation or during a scheduled follow-up testing session. Total testing time for the first and second phases of the study was approximately 1.5 hours.

The final phase of the study consisted of testing children on the smooth pursuit eye movement task. This testing was performed during a follow-up testing session because of limited availability of the eye-movement measurement apparatus. This phase of testing took approximately five minutes to complete.

All appointments for testing (phases I-II and phase III) were scheduled during the late afternoons and weekends to maximize the possibility that children with ADHD were not taking stimulant medications. Although some researchers have failed to find significant differences on measures of executive functions between children with ADHD on or off medications (Seidman et al., 1997), this design helped to ensure that differential test results between children with ADHD and normal controls were not reduced secondary to the effects of medication. At the same time, the design of this study minimized the need for any change in the child's medication regimen.

CHAPTER 3
RESULTS

All statistical analyses were conducted using SPSS for Windows, Release 9.0.1 (SPSS, 1999). Of the 71 subjects recruited for the study, 62 were included in the final analyses. Five subjects failed to complete the study because of time constraints of the primary caregiver or disinterest on the part of the child, two subjects were excluded because of failure to meet the WISC-III FSIQ cut-off, one subject was excluded for having a comorbid neurological condition (i.e., epilepsy), and one subject was excluded because of incomplete data (secondary to computer malfunction). No children were excluded based on the WRAT3 Spelling percentile score cut-off. Only one of these children would have met Barkley's (1998) rigorous definition of LD (i.e., a discrepancy of $\geq$ 15 points between expected and actual achievement scores and a score $\geq$ 1.5 standard deviations below the mean on an achievement test).

Each variable in the remaining 62 subjects was scanned for missing data. Eight variables were found to have missing data points, with a maximum of 3 missing data points per variable. These points were missing because of computer program malfunction or tester error. Data points were replaced based on a regression method (linear trend at point; SPSS 9.0.1). In order to ensure that the data of all subjects who participated in the study were used in the final analyses regardless of whether or not they had some missing data points, replacement of data points was chosen rather than

employing listwise deletions. Linear trend at point was chosen as the replacement method because each individual's missing value is predicted using a regression method.

After all missing data points were replaced and the data set was complete, the assumption of normality was assessed for each variable. Each dependent variable was evaluated for evidence of symmetry in its distribution using a test of skewness. A cut-off point of 2.0 was applied to the test of skewness as indicative of normality. Non-normal data were normalized using logarithmic transformations. All computerized attention measure variables (i.e., # hits, # misses, # false alarms and # false presses to both the sustained attention task and the shifting attention tasks) failed to meet the assumption of normality and were transformed to more closely approximate this assumption. Additionally, the number of saccades during smooth pursuit required logarithmic transformation to more closely approximate the assumption of normality. None of the screening variables (i.e., WISC-III FSIQ, WRAT3 Reading percentile, or Parent Conners ADHD Index) nor the Stroop Interference score required logarithmic transformation.

Demographics

Following replacement of missing data and transformations of skewed data, independent samples t-tests were used to test the differences between the children diagnosed with ADHD and the normal control group on demographic and screening characteristics. A comparison of the two groups' demographic information is presented in Table 5. The mean age of the ADHD group was 10.1 years (range 8 years, 2 months to 12 years, 6 months), while the mean age of the normal control group was 9.8 years (range 8 years to 11 years, 11 months). There were 20 boys and 11 girls in the ADHD group,

and a comparable 22 boys and 9 girls in the normal control group. The two groups did not differ significantly in sex, age, grade, parent education level, or parent income.

Table 5
Comparison of Demographic Variables Across Groups

Variable	Group ADHD mean (SD)	Group Control mean (SD)	Test statistic chi-square[a] t[b-d] Mann-Whitney[c]	p
[a]Sex	20 M, 11 F	22 M, 9 F	.032	.86
[b]Age	10.1 (1.2)	9.8 (1.2)	.956	.34
[c]Current Grade	3.97 (1.7)	3.87 (1.3)	.304	.76
[d]Parent Education	14.4 (2.0)	15.2 (1.5)	-1.695	.10
[e]Family Income	5.85 (1.48)	6.07 (1.15)	449.5	.64

Scores on screening measures including the Conners' Parent Rating Scale, WISC-III, and WRAT3 were also compared across the two groups (see Table 6). As expected given that the Conners' Parent Rating Scale ADHD Index score was one of three criteria used to define ADHD subjects for this study, there was a significant difference between the means of the two groups. Specifically, the mean t-score on the ADHD Index for the ADHD group was 76.4 (SD = 8.5) and significantly higher than the mean t-score of 48.7 (SD = 7.0) in the normal control group ($t_{(60)} = 13.981$, $p < .000$). The mean estimated WISC-III Full Scale IQ (FSIQ) of the ADHD group was significantly lower than the mean FSIQ of the normal control group ($t_{(60)} = -3.249$, $p < .002$). ADHD subjects earned a mean estimated FSIQ score falling in the Average range (FSIQ = 101.5), while control

subjects earned a mean estimated FSIQ falling in the High Average range (FSIQ = 113.7). Although the two groups differed significantly on FSIQ, this variable was not entered as a covariate in the initial analyses. Many researchers have argued against covarying IQ given that intellectual deficits may be an integral part of the ADHD disorder (Carte et al., 1996; Seidman et al., 1997). Furthermore, research does not support an expectation of differences in attentional abilities between children with average FSIQs versus those with high average FSIQs (Kaplan, Crawford, Dewey, & Fisher, 2000).

Table 6

Comparison of Screening Variables Across Groups

	Group		
Variable	ADHD	Control	t
Parent Conners' ADHD Index	76.4 (8.5)	48.7 (7.0)	13.981[1]*
Estimated WISC-III Full Scale IQ (FSIQ)	101.5 (13.6)	113.7 (15.8)	-3.249*
WRAT3 Spelling percentile	43.7 (21.8)	68.5 (23.9)	-4.281*

* $p < .002$

The mean estimated WRAT3 Spelling Subtest percentile score of the ADHD group was also significantly lower than the mean Spelling Subtest percentile score of the normal control group ($t_{(60)} = -4.281$, $p < .000$). Although the two groups differed significantly on their achievement screening scores, this variable was also not entered

into further analyses as a covariate because both groups' mean scores fell within the average range, suggesting clinically similar performances.

Statistical Analyses

Hypothesis 1

A one-way multivariate analysis of variance MANOVA, with two levels of the independent variable was employed to test the hypothesis that children diagnosed with ADHD would score significantly worse than healthy controls on computerized sustained attention tasks. The six dependent variables were the log transformations of the number of misses, false alarms, and false presses on both the first and second sustained attention tasks. Hits and misses have a 1-to-1 inverse relationship, therefore only misses (representing omission errors) were entered into the MANOVA. (The actual correlation between hits and misses was .934 for the first sustained attention task and .995 for the second sustained attention task. (Correlations did not reach 1.0 because of computer scoring errors of less than or equal to one target item on each task.) False alarms and false presses were both entered into the MANOVA as they represent different types of commission errors. Group means and standard deviations (prior to log transformations) for the measures of sustained attention are presented in Table 7. The MANOVA revealed a significant multivariate between-group difference $F(6, 53) = 2.938$, $p < .015$, with a medium multivariate effect size (partial eta-squared) = .25 (observed power = .861).

Post-hoc univariate tests showed that three of the six sustain attention variables hypothesized to discriminate the groups were different across the two groups using the Bonferroni adjustment. These variables were number of misses, false alarms, and false presses during the second sustained attention task. The exceptions were the number of

misses, false alarms, and false presses during the first sustained attention task. Number of misses during the first sustained attention task was significantly different between groups at a level of $p < .009$, but failed to meet the Bonferroni adjustment. Similarly, the number of false presses during the first sustained attention task was significantly different between groups at a level of $p < .028$, but also failed to meet the Bonferroni adjustment. Effect sizes (partial eta-squared) for the significant variables ranged from .119 to .197 and are presented in Table 8. In summary, when compared to the normal control children, the children with ADHD exhibited significantly more misses, false alarms, and false presses on the second sustained attention measure.

Table 7
Group Scores on the Computerized Measures of Sustained Attention

	ADHD			Control		
	N	Mean	SD	N	Mean	SD
Sustained Attention 1:						
Misses	31	4.5	4.0	31	2.3	2.7
False Alarms	31	1.2	1.8	31	0.6	1.0
False Presses	31	9.5	9.3	31	3.9	2.8
Sustained Attention 2:						
Misses	31	11.4	10.3	31	4.6	4.8
False Alarms	31	2.4	4.8	31	0.3	0.6
False Presses	31	15.9	28.0	31	1.7	2.6

Table 8

Effect Sizes for Significant Sustained Attention Variables

	Effect Size
Sustained Attention 2:	
Misses	.119
False Alarms	.197
False Presses	.194

Hypothesis 2

A separate one-way MANOVA, with two levels of the independent variable was employed to test the hypothesis that children diagnosed with ADHD would score significantly worse than healthy control children on a computerized measure of shifting attention. For this analysis, the six dependent variables entered into the analysis were the log transformations on the ratios of the number of actual responses to the number of possible responses. Ratios rather than raw scores were used because the number of possible responses varied depending on the child's response pattern and ratios equate the percentage of possible responses across subjects. For example, a subject who frequently responded incorrectly might have 50 possible targets. Therefore, 25 hits (25 misses) represents only 50% accuracy. Alternatively, a subject who responded more accurately might have 30 possible targets, such that 25 hits (5 misses) represents 83% accuracy. Therefore, a log transformation was conducted on the number of actual misses divided by

the number of possible misses, on the number of actual false alarms divided by the number of possible false alarms, and on the number of actual false presses divided by the number of possible false presses. Six ratios (misses, false alarms, and false presses for the first and second shifting attention sets) were entered into the MANOVA, with group as the independent variable. Group means and standard deviations (prior to log transformations) of the ratios for the measures of shifting attention are presented in Table 9. The MANOVA revealed a significant multivariate between-group difference $F(6,53) = 3.694$, $p < .004$, with a medium multivariate effect size (partial eta-squared) = .295 (observed power = .937).

Post-hoc univariate tests showed that three of the six shifting attention variables hypothesized to discriminate the groups were different across the groups using the Bonferroni adjustment. These variables were false alarms during the first shifting attention task and misses and false alarms during the second shifting attention task. The exceptions were the number of misses and false presses during the first shifting attention task, and number of false presses during the second shifting attention task. Number of misses during the first shifting attention task was significantly different between groups at a level of $p < .032$, but failed to meet the Bonferroni adjustment. Similarly, the number of false presses during the second shifting attention task was significantly different between groups at a level of $p < .022$, but also failed to meet the Bonferroni adjustment. Effect sizes (partial eta-squared) for the significant variables ranged from .142 to .188 and are presented in Table 10. In summary, when compared to the normal control children, the children with ADHD exhibited significantly more false alarms on

the first shifting attention task and significantly more misses and false alarms on the second shifting attention task.

Table 9
Group Ratios on the Computerized Measures of Shifting Attention

	ADHD			Control		
	N	Mean	(SD)	N	Mean	(SD)
Shifting Attention 1:						
Misses	31	13	(9)	31	8	(7)
False Alarms	31	16	(15)	31	7	(8)
False Presses	31	3	(7)	31	1	(2)
Shifting Attention 2:						
Misses	31	20	(15)	31	8	(10)
False Alarms	31	19	(17)	31	7	(1)
False Presses	31	6	(11)	31	1	(2)

Hypothesis 3

An independent t-test was employed to test the hypothesis that the children diagnosed with ADHD will score significantly lower than controls on the interference portion of the Stroop. Results of this analysis failed to find significant differences between the two groups. Specifically, the mean t-score on the Stroop for the ADHD group of 48.71 (SD = 3.92) was not significantly different than the mean t-score of 47.87 (SD = 4.54) in the normal control group ($t_{(60)} = .774$, $p < .442$).

Table 10
Effect Sizes for Significant Shifting Attention Variables

	Effect Sizes
Shifting Attention 1:	
False Alarms	.142
Shifting Attention 2:	
Misses	.188
False Alarms	.161

Hypothesis 4

Another independent t-test was employed to test the hypothesis that children diagnosed with ADHD will exhibit a significantly greater frequency of saccades versus healthy control subjects during a smooth pursuit task. A subset of 18 ADHD subjects and 18 normal controls was used for the comparison. Only 18 of the 31 ADHD subjects completed the eye-movement task while stimulant medication free. Because it is unclear whether or not stimulant medication affects control of eye-movements, only data from medication free subjects were used for this analysis. In order to maintain an equal number of subjects in each group, control subjects were matched for age and sex. Results of the independent samples t-test indicated that the groups were not different with regard to their performance on the smooth pursuit task. Specifically, ADHD subjects displayed an average of 1.7 anticipatory saccades during the smooth pursuit task which is not

significantly different from the average of 2.1 anticipatory saccades displayed by the control subjects ($t_{(34)} = -.716$, $p < .479$).

Hypotheses 5 & 6

Pearson correlation coefficients were calculated to test the hypotheses that a) performance on the shifting attention task was negatively correlated with the frequency of saccades made during the smooth pursuit task and b) the Stroop interference score was positively correlated with performance on the sustained attention task. The impetus for this analysis followed from the hypotheses that measures of frontal lobe functioning (i.e., the Stroop and computerized sustained attention measures) would be highly correlated with each other. Similarly, measures of cerebellar functioning (i.e., the eye-movement task and computerized shifting attention measures) would be highly correlated, yet not correlated with measures of frontal lobe functioning. Results from the correlation matrix indicated that neither the Stroop, nor the frequency of saccades during smooth pursuit, was significantly related to any of the computerized attention measure variables.

Additional Analyses

To clarify the relative contribution of each of the measures toward discriminating the ADHD group from the normal control group, a discriminant function analysis was conducted. Tests of homogeneity of the covariance matrices revealed that the groups are not homogenous with respect to covariance matrices (Box's M = 78.04, F = 3.295, p<.000) However, because the groups contain adequate sample sizes, there is only a minimal possibility that observations may be over classified into the group with the larger covariance matrix. The impact of a possible violation of multicollinearity among independent variables was reduced by employing an "enter together" technique rather

than a "stepwise" technique. A simultaneous estimation method was employed to derive the discriminant function. The independent variables used to predict group membership were the following six variables that were significantly different between the children with ADHD and the normal controls:

- log transformation of misses during the second sustained attention task (log miss - sustain2)
- log transformation of false alarms during the second sustained attention task (log false alarm - sustain2)
- log transformation of false presses during the second sustained attention task (log false presses - sustain2)
- log transformation of false alarms during the first shifting attention task (log false alarms - shift1)
- log transformation of misses during the second shifting attention task (log misses - shift2)
- log transformation of false alarms during the second shifting attention task (log false alarms - shift2)

Tests of statistical significance revealed only one derived discriminant function (Wilks' Lambda = .675, $p<.002$). The equation, which best discriminates the groups can be calculated as - .378 (log miss - sustain 2) + .047 (log false alarm - sustain2) + .543 (log false presses - sustain2) + .183 (log false alarms - shift1) + .60 (log misses - shift2) + .40 (log false alarms - shift2). Classification results indicated a hit ratio of 79% of the original grouped cases, such that 23 of the 31 ADHD children were correctly classified. In other words, eight children diagnosed with ADHD were misclassified as children in

the control group, resulting in a false negative rate of 25.8%. Twenty- six of the 31 children in the control group were correctly classified, resulting in a false positive rate of 16.1%. The classification results are summarized in Table 11.

Table 11
Discriminant Function Classification Results

		Predicted Group Membership		
	Group	ADHD	Control	Total
Count	ADHD	23	8	31
	Control	5	26	31
%	ADHD	74.2	25.8	100
	Control	16.1	83.9	100

CHAPTER 4
DISCUSSION

The present study was designed to examine sustained and shifting attention abilities in children with ADHD compared to a normal control group. While research clearly supports the hypothesis that children with ADHD show deficits on measures of sustained attention (Grodzinsky & Diamond, 1992; Mataro et al., 1997), less is known about their ability to rapidly shift attention within a single sensory modality.

In addition to assessing the performance of children with ADHD on sustained and shifting attention tasks, this study was designed to support the hypothesis that deficits in ADHD are due to dysfunction in multiple neuroanatomical regions, including frontal and cerebellar regions. The literature reviewed clearly indicates that children with ADHD perform poorly on measures of executive functioning (including measures of sustained attention) which are known to be sensitive to frontal lobe dysfunction (Lezak, 1995). Additional support of the hypothesis that children with ADHD exhibit frontal lobe dysfunction comes from neuroimaging studies with results indicating that children with ADHD show decreased size and hypoperfusion of the frontal lobes when compared to normal control children (Bush et al. 1999; Castellanos et al., 1996; Filipek et al., 1997; Hynd et al., 1990; Vaidya et al., 1998; Zametkin et al., 1993). While results of neuroimaging studies clearly implicate frontal lobe dysfunction in children with ADHD, many studies show abnormalities in other neuroanatomical regions. These regions include subcortical structures (e.g., globus pallidus, caudate, and striatum) as well as the

cerebellum (Berquin et al., 1998; Castellanos et al., 1996; Castellanos et al., 2001; Mostofsky, Reiss, Lockhart, & Denckla, 1998).

In contrast to the our ability to support the notion of frontal lobe dysfunction in children with ADHD with neuroimaging as well as neuropsychological studies, there are few neuropsychological measures available to assess cerebellar functioning. One such measure, shown to implicate the cerebellum is the computerized measure of shifting attention utilized in this study (Le et al., 1998). Therefore, measures of sustained and shifting attention were used not only to show that children with ADHD exhibit dysfunction on these types of tasks, but also to support the hypothesis that deficits in ADHD are due to dysfunction in a variety of neuroanatomical regions, including the frontal lobes and cerebellum.

In order to lend support to the hypothesis that poor performance on the sustained and shifting attention tasks is due to frontal and cerebellar dysfunction, respectively, children were administered additional tasks known to be sensitive to dysfunction in each region. Specifically, their performance on the Stroop (a measure previously shown to be sensitive to frontal lobe dysfunction) and on a smooth pursuit eye-movement task (a measure previously shown to be sensitive to cerebellar dysfunction) was correlated with their performance on the computerized measures of sustained and shifting attention.

Demographics

One of the strengths of this study was the strict inclusionary/exclusionary criteria employed. As indicated above, all children in the ADHD group met two of three criteria for diagnoses. Additionally, children in the ADHD group were free of any other disorders (with the exception of ODD). There were no significant differences between

the groups with regard to age, sex, current school grade, parent education level, or parent income. Therefore, group differences on the experimental tasks cannot be attributed to demographic differences. There were multiple benefits of restricting the age range to between 8 and 12 years. These included helping to ensure that children were developmentally capable of completing the computerized tasks (Akshoomoff and Courchesne 1994) and helping to ensure that children had already undergone a period of rapid development in executive function abilities (Welsch et al., 1989). However, because of the restricted age range of the subjects, the results of this study cannot be generalized to the full range of children diagnosed with ADHD. The limited generalizability of the results of this study will be discussed further in the sections that follow.

While group differences cannot be attributed to demographic differences between the groups, it may be suggested that differential performance on the sustained and shifting attention tasks is secondary to statistically different FSIQ scores between the groups. FSIQ was not entered into the primary analyses as a covariate because researchers have argued against covarying IQ given that intellectual deficits may be an integral part of the ADHD disorder (Carte et al., 1996; Seidman et al., 1997). Additionally, research does not support an expectation of differential attentional abilities between children with average FSIQ scores and those with high average FSIQ scores like those in this study (Kaplan et al., 2000; Spivak et al., 1997). Nonetheless, the FSIQ scores of the two group were significantly different. Therefore, post-hoc analyses were conducted comparing the two groups on the measures of sustained and shifting attention while covarying FSIQ. To ensure that FSIQ differences were not confounding our

results, FSIQ was covaried out of the MANOVA's for sustained and shifting attention. The resulting sustained attention MANCOVA revealed a significant multivariate between group difference $F(6, 52) = 2.224$, $p < .05$. Two of the three sustained attention variables shown to discriminate the groups using MANOVA remained significant after covarying for FSIQ. These two variables were false alarms and false presses during the second sustained attention task. Number of misses during the second sustained attention task was significantly different between the groups at a level of $p<.038$, but failed to meet the Bonferroni adjustment. The resulting shifting attention MANCOVA revealed a significant multivariate between group difference $F(6, 52) = 2.544$, $p < .031$. Again, two of the three shifting attention variables shown to discriminate the groups using MANOVA remained signiticant after covarying for FSIQ. These two variables were misses and false alarms during the second sustained attention task. Number of false alarms during the first shifting attention task was significantly different between the groups at a level of $p<.011$, but failed to meet the Bonferroni adjustment. Therefore, results of post-hoc analyses indicated that covarying for FSIQ had little impact on revealing group differences on sustained and shifting attention measures.

Sustained Attention

As expected, children with ADHD performed significantly worse than normal controls on measures of sustained attention. Consistent with prior research, children with ADHD exhibited significantly more omission errors (misses) as well as commission errors (false alarms and false presses). However, significant differences between the groups were only evident on the second sustained attention task. As target feature attended to (i.e., color versus shape) during the first and second sustained attention tasks

was counterbalanced across subjects, impaired performance on the second shifting attention task by children with ADHD cannot be attributed to target type.

While there was a trend toward significant differences between the groups on measures of sustained attention during the first sustained attention task, results (i.e., significant differences between the groups on only the second sustained attention task) suggest two important points. First, differences between the groups cannot be attributed to a differential ability to understand the task directions. In other words, as the performance of children with ADHD was not significantly different from the performance of normal control children on the first sustained attention measure, groups appeared to have similar understanding of task directions. Second, results are consistent with prior studies showing that children with ADHD perform poorly not only on when required to inhibit an unwanted response, but also when vigilance (i.e., the ability to wait for increasingly longer periods of time for infrequently occurring events) is required (Fletcher, 1998).

As indicated, results showed that children with ADHD exhibited significantly more misses, false alarms, and false presses than normal control children on the second sustained attention task. These results are consistent with the theory of ADHD that purports that these children appear inattentive as a result of poor inhibition mechanisms that result in an inability to resist distraction (Barkley, 1997). As such, children with ADHD are drawn off task, either by internal or external distractions. External distractions may be intrinsic to the task at hand (i.e., distractors related or unrelated to the target) or in the surrounding environment. These poor inhibition mechanisms result in an increased tendency to respond falsely to distractors (both related and unrelated to the

target) and an increased tendency to miss targets when compared to normal control children.

The aforementioned errors are comparable to the types of problems frequently noted in children with ADHD. For example, a child with an increased tendency to respond falsely to intrinsic, related distractors may exhibit behaviors such as skipping ahead while reading a story. Similarly, a child with an increased tendency to respond falsely to intrinsic, unrelated distractors may focus on the pictures in a book when he/she is supposed to be focused on the text. Additionally, children who exhibit an increased tendency to miss targets due to internal distractions or external distractions in the surrounding environment may be observed to be playing with objects (e.g., pencils or erasers) or attending to their peers rather than attending to the assigned task.

Finally, it is important to note that as expected, significant differences between the two groups on measures of sustained attention were found even with 5 of 31 children on stimulant medication at the time of testing. While it is not known whether these children would have performed more poorly on the computerized sustained attention tasks off medication, results suggest that the measure may be sensitive to ADHD dysfunction regardless of medication status.

Shifting Attention

A computerized measure of shifting attention was developed for this research based on the task used by Akshoomoff and Courchesne (1994). This shifting attention task was similar to the computerized sustained attention task with one additional component of requiring the subjects to shift their attention between two targets (color and shape) rather than maintaining attention to a single target (color or shape). Results of this

study, comparing the performance of children with ADHD to healthy control children on this measure of shifting attention indicated that, as hypothesized, the children with ADHD performed significantly worse. While it may be suggested that the children with ADHD performed significantly worse as a result of an increased need to sustain attention due to the complexity of the task, results suggest otherwise. The two groups were significantly different on three of six measures of shifting attention. Two of these measures, number of false alarms committed on either the first or second shifting attention task, are measures of the number of times the child mistakenly responded to the same target twice in a row (i.e. forgot to shift). The poorer performance of the ADHD children on this particular measurement indicates that they exhibited deficient intramodality shifting skills.

The only other studies to evaluate intramodality shifting attention skills in children with ADHD employed the WCST as a measure of shifting attention. While the performance of children with ADHD was frequently compared to normal control children on measures such as the number of categories completed, the number of failures to maintain set, and the number of trials required to obtain the first category, these measures do not assess shifting attention. Rather, they measured constructs such as disinhibition and problem solving. As Barkley and colleagues (1992) suggest in their review of executive functions, in order to address the construct of shifting attention when employing WCST, number of perseverative errors must be evaluated. Results from this study are consistent with the studies that compared number of perseverative errors exhibited on the WCST by children with ADHD and normal controls. In those studies, as well as the present study, children with ADHD exhibited deficient intramodality shifting

skills compared with normal a control group. The benefit of using the current computerized task (rather than the WCST) as a measure of shifting attention is that the requirement to shift between targets is clearly delineated for the subjects. Each child is explained the shifting rule and provided an opportunity to express understanding of that rule. Alternatively, on the WCST, the child must determine the shifting rule based on examiner feedback. Additionally, the shifting rule frequently changes throughout the task without explanation. Therefore a failure to shift on the WCST may be a result of a failure to comprehend the higher order task demands, whereas failure to shift on the current computerized measure can be hypothesized to result from fundamental poor attention shifting skills.

The third measurement indicating that children with ADHD performed significantly worse than the normal control group was a measure of omissions (i.e., "misses") on only the second shifting attention task. Similar to the results found on the measure of sustained attention, the increased tendency of the children with ADHD to miss targets on only the second task when compared to the normal control children again suggests decreased attention over increasingly longer period of time (i.e., poor vigilance).

The results of this study suggest important implications for working with a child with ADHD. Specifically, a child who exhibits difficulty with intramodality shifting may have difficulty in the classroom when required to switch between tasks. Even if the child can verbalize the directions for shifting, s/he may have difficulty executing the switch.

Finally, it is again important to note that as expected, significant differences between the two groups on measures of shifting attention were found even with 5 of 31 children on stimulant medication at the time of testing. While it is not known whether

these children would have performed more poorly on the computerized shifting attention tasks off medication, results indicate that the measure is sensitive to ADHD dysfunction regardless of medication status.

Stroop Test

As indicated above, one goal of this study was to support the hypothesis that children with ADHD exhibit dysfunction on measures of frontal lobe functioning. In addition to the computerized sustained attention task, the Stroop was employed in the current study as a measure of frontal lobe functioning for two reasons. First, Lezak's review (1995) indicated that this measure is highly sensitive to frontal lobe functioning. Second, a review of the literature indicated that 5 of 6 early studies (Barkley, Grodzinsky & DuPaul, 1992) and 3 of 3 more recent studies (Grodzinsky & Diamond, 1992; Seidman et al., 1997; Semrud-Clikeman et al., 2000) found significant differences between children with ADHD and normal controls on the Stroop. Taking these two points together, it was hypothesized that children with ADHD (who have been shown to exhibit frontal lobe abnormalities) would perform significantly worse than normal control children on the Stroop. However, this hypothesis was not confirmed. Rather, no significant differences between the two groups were found on the interference portion of the Stroop.

There are a number of possible reasons for the discrepant results between this and past research. First, there were differences across the studies with regard to the specific dependent variable used to make group comparisons. For example, some studies used the time to complete the interference portion of the task, some studies used the number of errors on the task, and some studies used scores from the non-interference portions of the

test (i.e., color, word, or color-word) in their statistical analyses. For this study, the interference score was used as the best measure of frontal lobe functioning. This score represents a child's approximation of his/her expected performance (actual score minus expected score) on the color-word condition relative to her/his speediness on each the word and color conditions. Time to complete the interference portion of the test or time to complete the color and word portions of the test were not used in this study because these scores assess response speed rather than a specific frontal lobe function (i.e., inhibition). Nonetheless, a one-way MANOVA, with two levels of the independent variable and three dependent variables (word t-score, color t-score, and color-word t-score) did reveal a significant multivariate between-group difference $F(3, 58) = 3.869$, $p < .014$. Consistent with the results from prior research, follow-up univariate analyses showed that the word and color t-scores were significantly different across the two groups. The fact that the ADHD group differed from the normal controls on the color and the word conditions means that they were slower in reading words and naming colors. This slowed performance undoubtedly affected their expected performance on the color-word condition as expected performance is figured by factoring in performance on the color and the word conditions (i.e., color + word / color * word). Therefore, children who perform more slowly on the color and word conditions are expected to perform more slowly on the combined (i.e., color-word) condition. Expecting less from children in the ADHD group might restrict the range of possible interference scores (i.e., actual color-word score - expected color-word score), thus, decreasing the variance in that group and limiting the likelihood of finding group differences in that analysis. Finally, increased power (i.e., larger sample sizes) and less stringent significance levels (i.e., .07 rather than

.05) may have allowed the investigators to find significant differences between the performance of children with ADHD versus normal control children on the interference portion of the Stroop.

Eye Movements

In addition to assessing frontal lobe functions in children with ADHD, a second goal of the present study was to assess the functioning of children with ADHD on measures of cerebellar functioning. Based on several neuroimaging studies showing cerebellar abnormalities in children with ADHD (Aylward et al., 1996; Castellanos et al., 1996; Filipek et al., 1997; Mataro et al., 1997; Vaidya et al., 1998), it was hypothesized that these children would be impaired compared to normal controls on measures of cerebellar functioning. In addition to the computerized shifting attention task, smooth pursuit eye-movements were employed in this study as a measure of cerebellar functioning based on previous research showing that patients with cerebellar damage exhibited deficient smooth pursuit skills. These smooth pursuit deficits included increased frequency of anticipatory saccades, initiation deficits, increased RMSE, and decreased smooth pursuit gain (Akshomoff et al., 1992; Bracke-Tolkmitt et al., 1989; Moschner et al., 1996; Straube et al., 1997; Vahedi et al., 1995).

Smooth pursuit eye-movements were assessed by having each child visually track a small target that moved horizontally back and forth over 30° with a constant velocity of 10°/second and a 1.4 second fixation between four changes in direction. Electro-ocular gram (EOG) recordings were used to collect eye movement information while the child performed the smooth pursuit tracking task. AcqKnowledge computer software

transformed the EOG data into sinusoidal wave forms representing the eye-movement patterns.

Contrary to the hypothesis that children with ADHD would exhibit significantly more anticipatory saccades than the normal control children, results did not reveal differences between the two groups. A number of factors may account for these negative findings. First and foremost, the negative results may be secondary to the use of qualitative rather than quantitative assessment procedures. The procedure for collecting eye movement data was changed in the beginning of the study. Originally, videos of corneal reflection were to be used to collect quantitative eye movement data. However, prior to running the first subject, it was determined that these methods were not able to be calibrated in children. In order to avoid losing subject data and risking the miscalibration of subjects because of age, we decided to use EOG recordings, allowing for only qualitative assessment of saccades. Due to this procedural change, frequency of saccades was calculated by counting the number of square wave deviations in the same direction as the slope (i.e., anticipatory saccades). Although independent raters achieved inter-rater reliability of .89 when counting frequency of saccades, saccades were judged based on qualitative rather than quantitative criteria. Quantitative criteria were not employed because inconsistent EOG voltage recordings were measured across subjects. As originally proposed, the exact position of the child's cornea with respect to target position was to be videotaped. Therefore, exact size and length of specific eye-movements were to be calculated. However, calibration difficulties precluded use of this procedure.

In addition to limitations from the procedure used, a failure to find significant results may have occurred because this analysis was underpowered. The estimated effect

was small (d = .25), which would require over 200 subjects in each group to detect group differences at the .05 level of significance with 80% power. The observed power with the current sample (N = 36) was 0.11.

Furthermore, a failure to find significant results may be secondary to the measurement procedure employed. Frequency of anticipatory saccades was chosen as a good measure of smooth pursuit dysfunction based on the high test-retest reliability of this measurement. Additionally, RMSE was to be calculated for each group as this was the only variable found to be significantly different between children with ADHD and normal control children in the one study that examined smooth pursuit eye-movements in children prior to the inception of this study (Jacobsen et al., 1996). Furthermore, in the one study that evaluated smooth pursuit eye-movement in children with ADHD since this study was conducted, RMSE was the only variable showing a trend toward significant difference between children with ADHD and normal control children (Castellanos et al., 2000). However, as the current procedure did not record target position relative to eye position, RMSE was not able to be calculated.

A failure to find significant differences between the two groups may also be due to the age of the subjects. Prior research suggests that differential performance on smooth pursuit tasks between patient and control groups may not be detectable until late adolescence as the smooth pursuit system does not fully develop until that time (Katsanis et al., 1998; Ross et al., 1993). These findings suggest that school age children, regardless of whether or not they are diagnosed with a disorder such as ADHD, may exhibit some deficits on smooth pursuit tracking and associated anticipatory saccades. Therefore, detecting significant differences between children with ADHD and control

subjects may be difficult until after the smooth pursuit system is full developed (i.e., late adolescence).

Overall Conclusions

Children with ADHD exhibited significant deficits on measures of sustained attention when compared to normal control children. They exhibited errors of both omission and commission. In other words, consistent with the theory that ADHD is a disorder of behavioral disinhibition (Barkley, 1997), children in this study exhibited poor interference control. This impaired interference control resulted in the children either missing targets (i.e., omissions) or falsely responding to distractors (i.e., commissions). Previous research clearly suggests that frontal lobe regions play a role in these sustained attention abilities (Pardo et al., 1991; Reuckert & Grafman, 1996; Zametkin et al., 1993). While the children with ADHD in this study were impaired on the computerized sustained attention task, one measure of frontal lobe functioning, they were not impaired on a second measure of frontal lobe functioning, the Stroop. Although results from this study are mixed with regard to performance of children with ADHD on measures of frontal lobe functioning, results from numerous other studies employing neuroimaging techniques and/or neuropsychological tests support the hypothesis of frontal lobe dysfunction in children with ADHD.

In addition to supporting previous research findings that children with ADHD show deficient sustained attention skills, this study is the first to provide specific evidence that children with ADHD also exhibit significant deficits on measures of intramodality attention shifting. While deficits on the sustained attention task were only evident after a relatively long period of responding (i.e., children with ADHD were only

significantly impaired on the second sustained attention task), children with ADHD exhibited deficits on both the first and second shifting attention task. More specifically, when compared to the normal control group, the children with ADHD evidenced significant difficulty shifting between two visual targets. Instead, they frequently responded to the same stimuli on subsequent trials. Previous research suggests that intramodality attention shifting skills may be controlled by the cerebellum (Akshomoff & Courchesne, 1994; Le et al., 1998). While intramodality attention shifting skills may be controlled by the cerebellum, results of the current study were unable to lend additional support to the hypothesis of cerebellar dysfunction in an ADHD population. Specifically, children with ADHD in this study were not significantly impaired on a measure of smooth pursuit eye-movements, a measure elsewhere shown to be sensitive to cerebellar functioning. While the children with ADHD were not impaired on the eye-movement task in this study when compared to the normal control children, additional research is necessary to clarify whether or not the children with ADHD exhibit eye-movement deficits and cerebellar dysfunction, more generally.

The computer tasks were the most robust and sensitive dependent variables in this study. Together, the sustained and shifting attention measures were able to correctly classify 80% of the subjects. These results are comparable to or exceed the results from prior studies that classified children as with or without ADHD based on their scores from a battery of neuropsychological tests (Barkley & Grodzinsky, 1999; Perugini, Harvey, Lovejoy, Sandstom, & Webb, 2000; Pineda, Ardila & Roselli, 1999). For example, Pineda and colleagues correctly classified 85% of their subjects using ten neuropsychological variables. Alternatively, Grodzinsky and Barkley were only able to

correctly classify 49-70% of their subjects using the scores of seven frontal lobe tests. Similar to the Grodzinsky and Barkley study which found the positive predictive power of the measures employed to range from 80 - 90%, results from this study indicated good positive predictive power (82%) These results suggest that abnormal scores may be indicative of the presence of ADHD. In contrast to the Grodzinsky and Barkley study which found the negative predictive power of the measures to range form 50 - 66%, results of this study also indicated good negative predictive power (76%). These results suggest that unimpaired scores are likely indicative of the absence of ADHD. Additionally, sensitivity and specificity were good at rates of 74% and 84%, respectively. The sensitivity of these measures may partially result from their inclusion of vigilance as a component of testing or to their strict focus on attention without including higher order executive functions. In either case, these tasks remain useful and promising for the future of ADHD research.

Future Research

In order to further our understanding of ADHD and thereby assist with the development of effective interventions, future research of children with ADHD should continue to focus on behaviors suspected to be deficient in an ADHD population and known to be associated with specific neuroanatomical regions. For example, additional studies should be conducted to further evaluate smooth pursuit eye-movements in children with ADHD. RMSE may be the best measure for assessing differences in children with ADHD and normal control children. Additional research on shifting attention skills in ADHD may evaluate their performance on inter-modality shifting attention tasks. Furthermore, future research evaluating the performance of children with

ADHD on measures of sustained and shifting attention should focus on the specific neuroanatomical correlates of the observed dysfunction. While it is possible that intramodality shifting is impacted by cerebellar dysfunction, it remains possible that this skill is primarily controlled by prefrontal regions. Therefore, studies that directly assess the neuroanatomical regions involved in the execution of sustained and shifting attention tasks are needed to better understand the dysfunction exhibited by children with ADHD. Direct assessment of the neuroanatomical regions involved in the execution of attention tasks can be completed using fMRI. For instance, using fMRI, in both ADHD and normal control populations, researchers may be able to assess which additional neuroanatomical regions are activated when an intramodality shifting component is added to sustained attention tasks.

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BIOGRAPHICAL SKETCH

Jill C. Gitten was born in Bronxville, New York on February 14, 1972 to Arnold and Bette Gitten. She has one older sister, Lisa Gitten. Jill was raised in Miami Florida where she graduated from Miami Sunset Senior High School in 1990. She then went to the University of Florida, in Gainesville, Florida, and earned a Bachelor's degree in Psychology in 1994. She returned to the University of Florida in 1995 as a doctoral student in the Department of Clinical and Health Psychology. Her primary area of study was neuropsychology with a focus on pediatric neuropsychology. After completing graduate studies at the University of Florida, she was fortunate to obtain a predoctoral internship in the Clinical Neuropsychology Track at the Brown University School of Medicine. She is currently at Brown University where she is a postdoctoral fellow in the Neurodevelopmental Center at Memorial Hospital.

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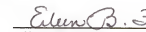

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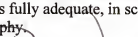

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